JOURNAL

OF THE

Indian Medical Association

VOLUME XXIII
NUMBER 12

CALCUTTA
SEPTEMBER 1954

Indian Medical Association
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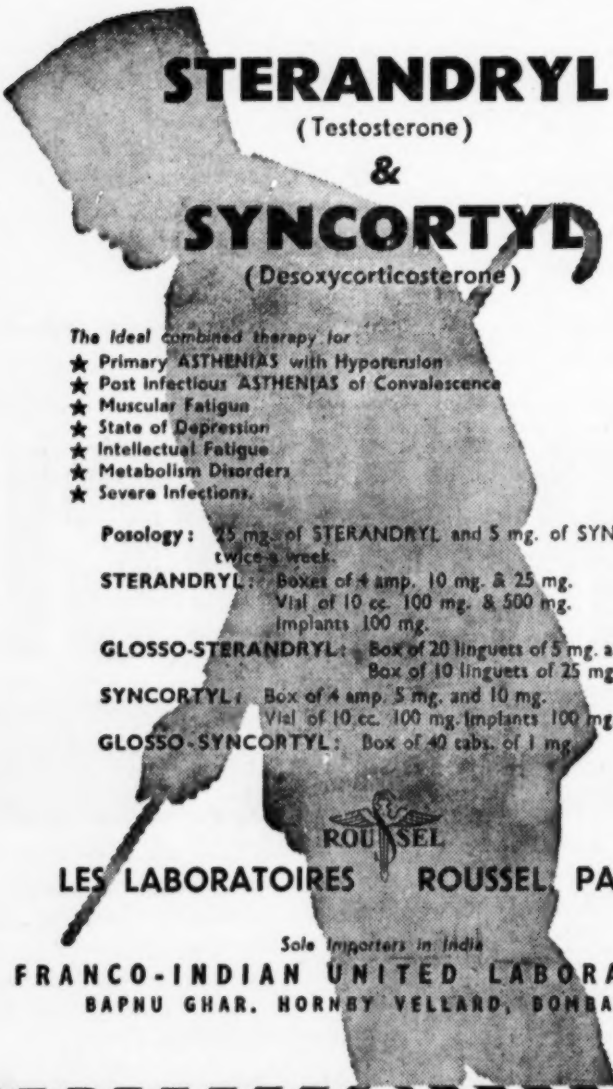

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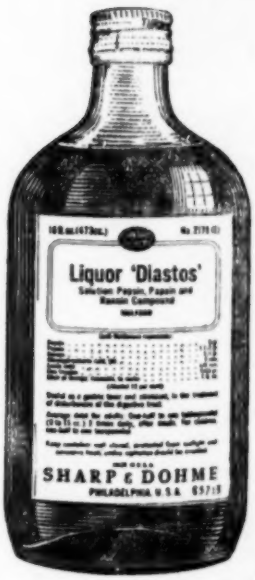

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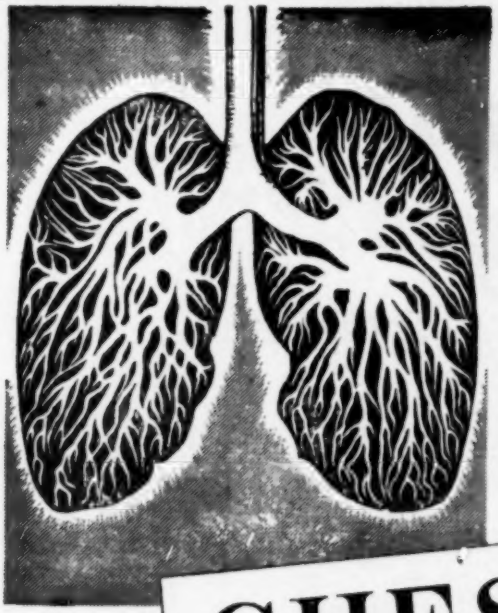

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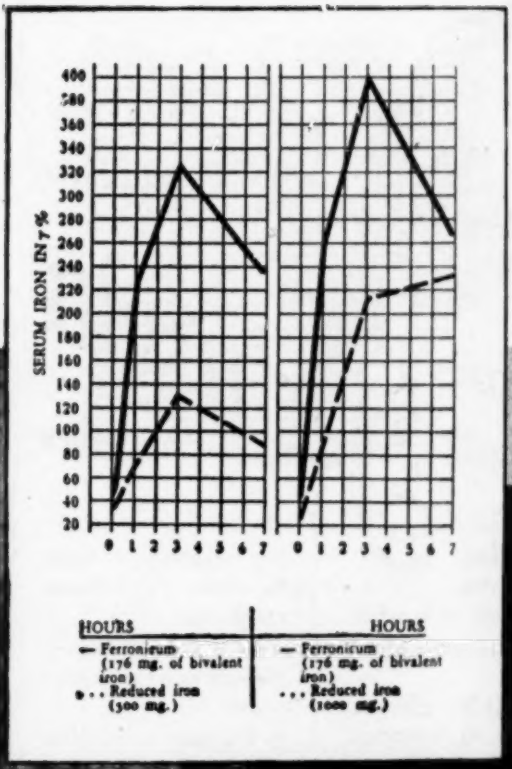

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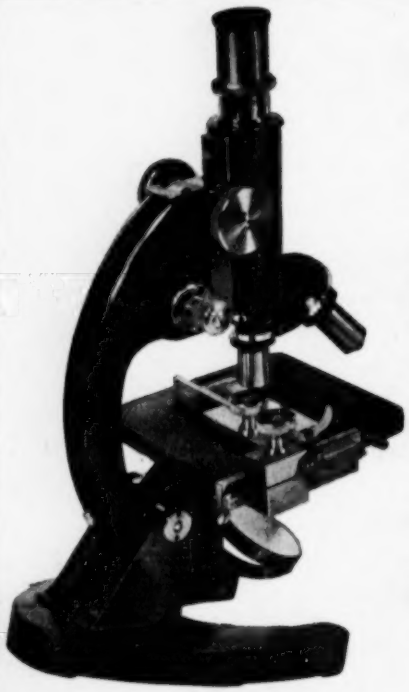

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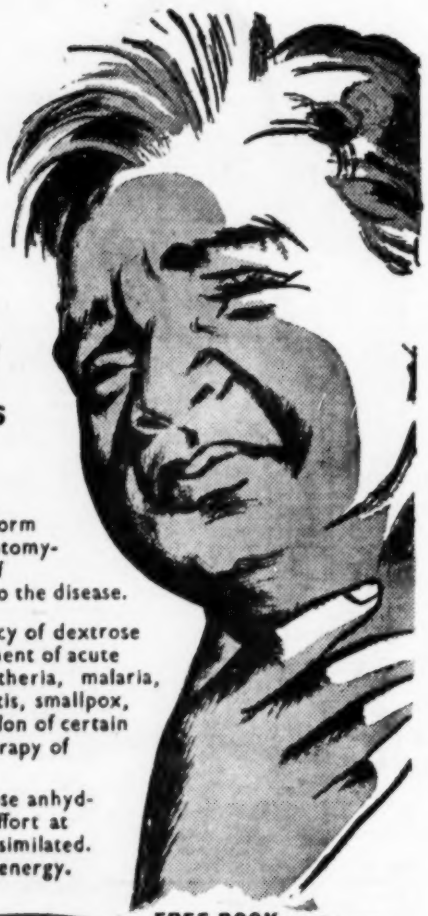

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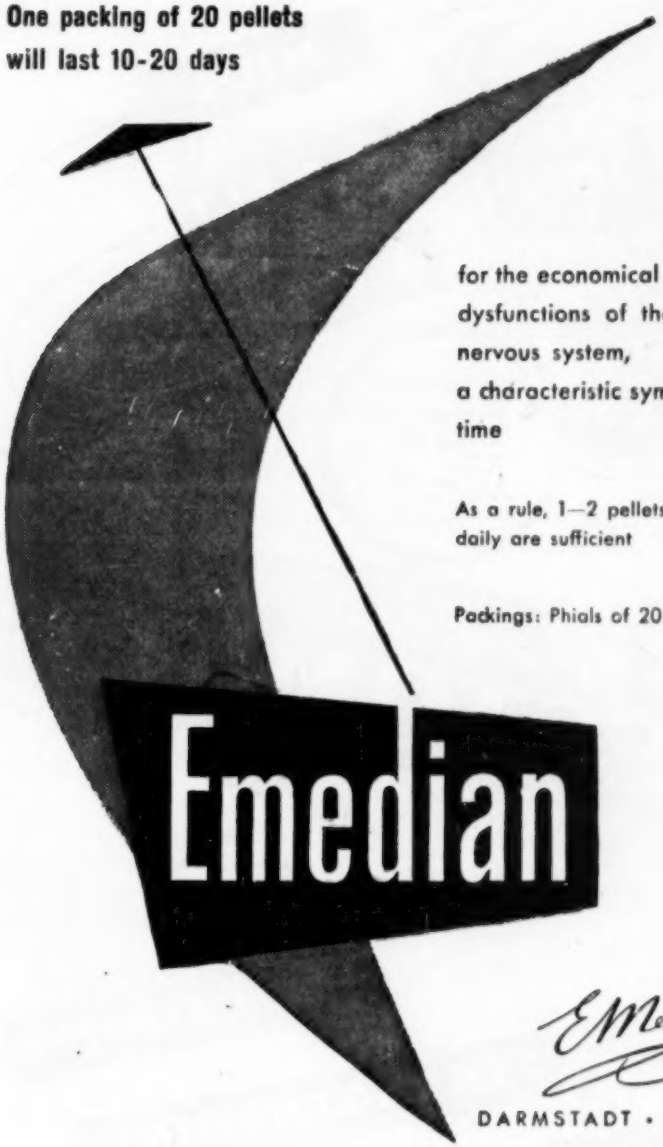

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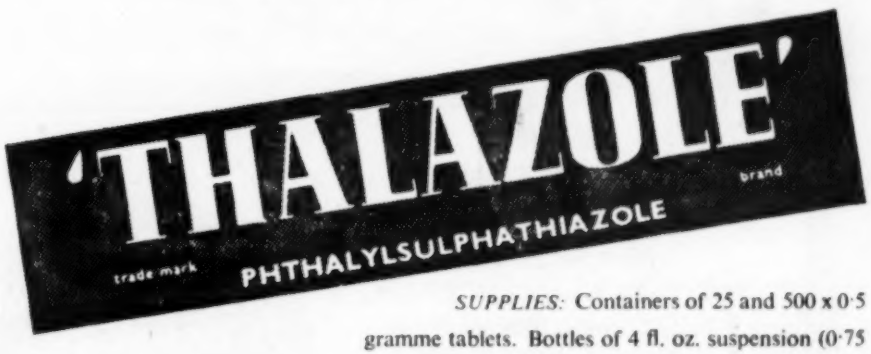

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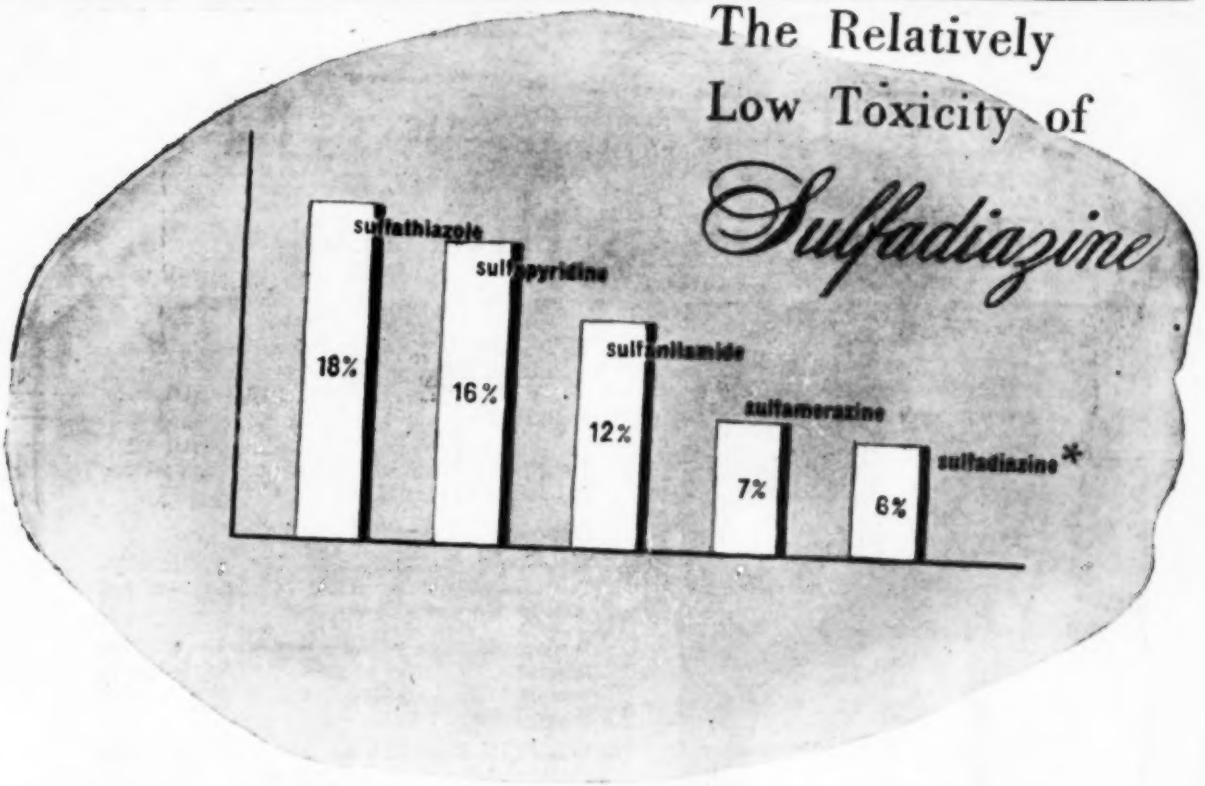

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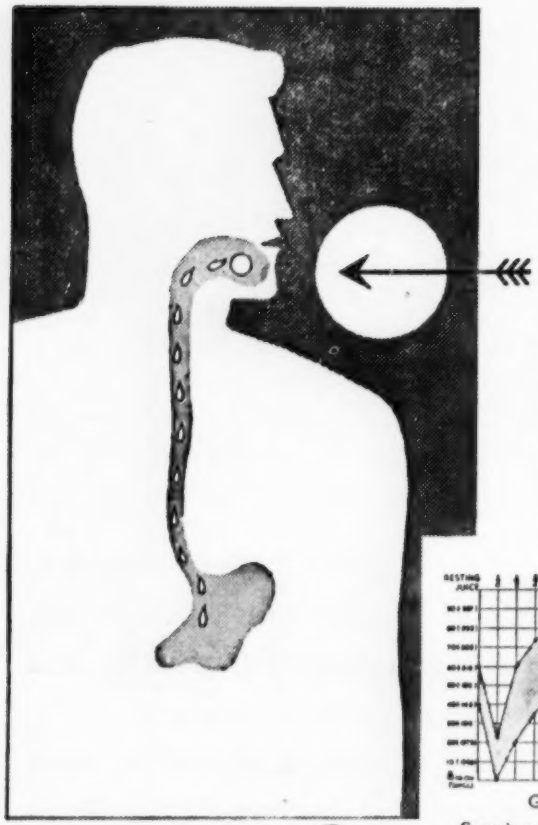

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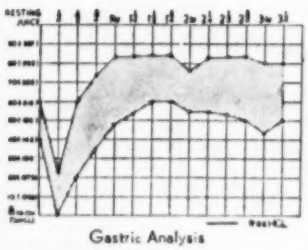
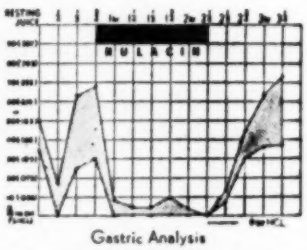


Gastric Analysis

Superimposed gruel fractional test-meal curves of five cases of duodenal ulcer.



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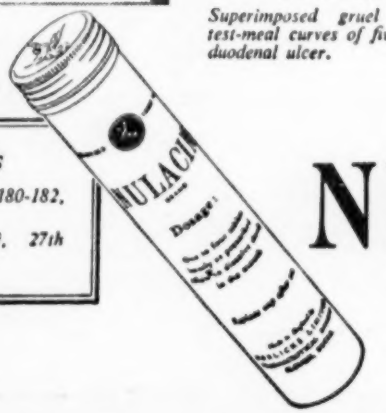

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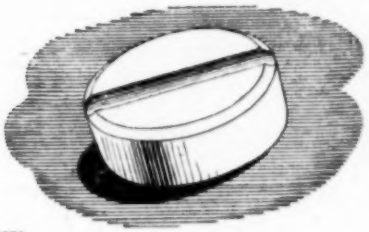

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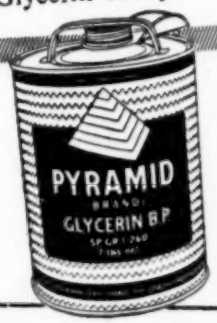

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Journal of the Indian Medical Association

VOL. XXIII, NO. 12 CALCUTTA SEPTEMBER, 1954

ORIGINAL ARTICLES

A CYTOCHEMICAL STUDY OF ENTAMOEBA HISTOLYTICA

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AND

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From the literature extant on the subject, very little information is available about the cytochemistry of *E. histolytica*. The references available to us indicate that desoxyribonucleic acid (DNA) could be demonstrated in the nucleus of the amoeba and that glycogen and acid phosphatase were present in the cytoplasm of the trophic form (Lillie, 1947; Carrera and Changus, 1948). In this article the results of our study of this amoeba utilising a number of modern histochemical methods are presented and their significance discussed. A preliminary note on some of our findings have already been published (Ray and Sen Gupta, 1954).

MATERIAL AND METHODS

The material studied consisted of (1) smears of specimen collected from cases of amoebiasis by sigmoidoscopy, faecal samples and cultures in Dobell's and in Row's media; and (2) tissue sections containing *E. histolytica*, viz., intestines, faeces of cases of amoebic dysentery.

The methods adopted were as follows:

1. Supravital staining with Janus green for mitochondria.

2. Supravital staining with neutral red for Golgi complex.

3. Feulgen's nucleal reaction.

4. Staining with pyronin and methyl green.

5. Modified Gomori methods for the localisation of alkaline and acid phosphatases (Glick, 1949; Pearse, 1953).

6. Bauer-Feulgen method for demonstration of glycogen (Glick, 1949).

7. Danielli's method for demonstration of aldehydes (Danielli, 1952).

8. Sudan IV stain for lipids (Lillie, 1948).

RESULTS

The results obtained and relevant technical details are presented below:

Mitochondria. The mitochondria were demonstrated by supravital staining of culture of *E. histolytica* with Janus green. A 0·40 per cent alcoholic solution of Janus green was used to make a thin smear on a clean slide; a drop of culture of amoeba on a cover slip was inverted on the smear on the slide and the edges sealed with hard paraffin.

The mitochondria were stained in 2-5 minutes and could be seen moving in the endoplasm along the cytoplasmic stream in the actively motile amoeba. In amoebae containing small food vacuoles, the mitochondria were seen to be arranged around the vacuoles. At first the mitochondria appeared green but within 2-5 minutes, the colour changed to purple or lavender or pink and this colour gradually faded and was completely discharged during the next 5-15 minutes. In a number of specimens of amoebae obtained from culture in Row's medium, the cytoplasm took a pink colour in about 5-10 minutes; this also faded and the amoebae regained the natural colourless form within the next 5-10 minutes. The large vacuole containing ingested starch grain showed that there were many (?) bacteria stained with Janus green which were showing very active movement around the starch grain. This could be observed for as long as 1½ hours when the contents of vacuole were seen to be expelled out of the cyto-

plasm of the amoeba. The contents of the vacuole seemed to undergo some sort of churning movement from time to time (Fig. 2, a and b).

Golgi complex. The Golgi complex could be visualised for several hours after supravital staining with neutral red. A 0·25 per cent alcoholic solution was used for making thin film of the dye on the slide.

The Golgi complexes were seen as spheroids in the endoplasm containing granules of neutral red under the phase contrast microscope. With the ordinary microscope, the spheroidal character of the complex was less obvious and the granules of neutral red could be seen to be moving in the endoplasm (Fig. 2, c and d). In the amoebae containing large starch grain in a vacuole, there was concentration of the dye in the vacuole which was stained deep orange.

Feulgen's nucleal reaction. Tissue sections fixed in Zenker's solution and smears fixed in Schaudinn, Serra or Zenker were used for the Feulgen reaction. Hydrolysis for 10 minutes at 60°C. was found to be adequate for smears and tissue sections containing the trophic form of the amoeba, but the period of hydrolysis could be extended to 20 minutes in a number of Serra and Zenker fixed specimens containing cysts with satisfactory results.

The nucleus of the trophic form showed Feulgen-positive granules arranged all along the nuclear membrane or more on one side of the membrane or showing the crescentic arrangement. The karyosome appeared as a dot or a hollow sphere with DNA containing material at the periphery. There were some minute granules of DNA in the nucleoplasm around the karyosome. Feulgen-positive material was similarly distributed in the nuclei of the cysts but staining of the nuclear membrane was at times very faint and occasionally the karyosome appeared very prominent. The endoplasm of the trophic form and the cyst at times gave an impression that it contained fine grains of DNA scattered all over. The chromatoid bars were found to contain DNA (Fig. 2, g and h).

Staining with methyl green and pyronin. Tissues were fixed in Carnoy or Zenker and smears in Serra or Carnoy for staining with Unna-Pappenheim stain or Brachet's pyronin-methyl green stain (1953). Another method (Sen Gupta *et al*, 1953) used was staining of wet preparations of cultures with methyl green and pyronin individually. A smear of alcoholic solution of the dye was allowed to dry on clean slide; a drop of culture of amoeba on a cover slip fixed by brief exposure to formalin vapour (1 to 2 minutes), was inverted on the smear of the dye and the edges of the cover slip sealed with hard paraffin. The specimen was examined when the amoebae were properly stained.

The distribution of DNA in the trophic form of the amoeba as judged by methyl green staining was similar to that noted with the Feulgen reaction (Fig. 2, e).

The structure of the chromatoid bar as revealed by Brachet's pyronin-methyl green stain was very interesting. These were found to contain varying proportions of both DNA and RNA containing material and the colour varied from red to purple and green. In some cysts the chromatoid bars showed an outer sheath of DNA and a bright red core of RNA containing material.

The cytoplasm was found to be very rich in RNA in both the trophic and the cystic forms: the endoplasm alone showing the specific staining for RNA, i.e., with pyronin. The nuclear membrane and the nucleoplasm were also stained with pyronin (Fig. 2, f). The cysts often showed fine methyl green staining particles in the cytoplasm.

Localisation of alkaline phosphatase. Smears wet-fixed in chilled 80 per cent alcohol or in acetone were used. It was necessary for the fixative to be kept at a temperature of 4°C. or less and to keep the koplin jar containing the smears in the fixative in ice bath for at least ½ hour. The smears were then transferred to 70 per cent alcohol and then to water before being put into the substrate. Modified Gomori method was used for demonstration of alkaline phosphatase and the period of incubation in 37°C. incubator was usually between 1 and 2 hours.

Alkaline phosphatase was found to be present mainly in the nucleus of the trophic form of *E. histolytica*; the endoplasm showed distinct but weaker reaction and the outer border of the ectoplasm also showed the presence of the enzyme (Fig. 1 and Fig. 2, i). In suitable specimens, a bilaminar distribution of alkaline phosphatase was noted, i.e., at the outer border of the ectoplasm there was a distinct deposit of cobalt sulphide, then there was a clear area followed by another layer of deposit of lesser density. This last layer appeared to correspond to the marginal layer of the endoplasm.

In the nucleus, the enzyme could be visualised as a series of granules along the inner aspect of the nuclear membrane; occasionally the granules were more on one side of the nucleus or even restricted to one side of the nucleus (crescentic arrangement). The karyosome was stained in almost all specimens and showed an intense reaction while the nucleoplasm at times exhibited a diffuse deposition of cobalt sulphide. The enzyme could be seen as fine granular deposit in the endoplasm. In a few specimens showing small food vacuoles, the enzyme was found located at the periphery of such vacuoles. The preparations made from sigmoidoscopic or faecal material showed more intense reaction for the enzyme in the endoplasm than those from 48 hour old cultures. In a cyst showing the mitotic figure, the chromosome number that could be made out at the telephase was six at each pole. The enzymic activity was intense in the chromosomes while the spindle fibres showed only a light reaction.

The cysts showed positive reaction for alkaline phosphatase in the nucleus but the intensity of reaction was very variable (Fig. 2, j and k). The cytoplasm showed weak reaction in most specimens but in

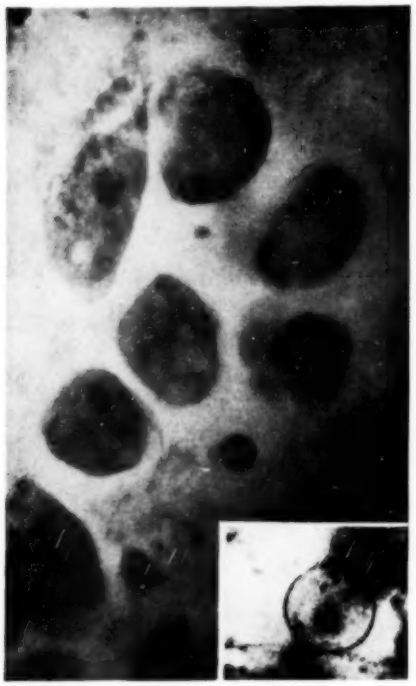

Fig. 1—Photomicrograph of a smear showing alkaline phosphatase reaction in *Entamoeba histolytica* × 800.

Inset photomicrograph of a cyst of *E. histolytica* showing alkaline phosphatase reaction × 1000. Note the granular deposit of cobalt sulphide at one pole of the spherical cyst.

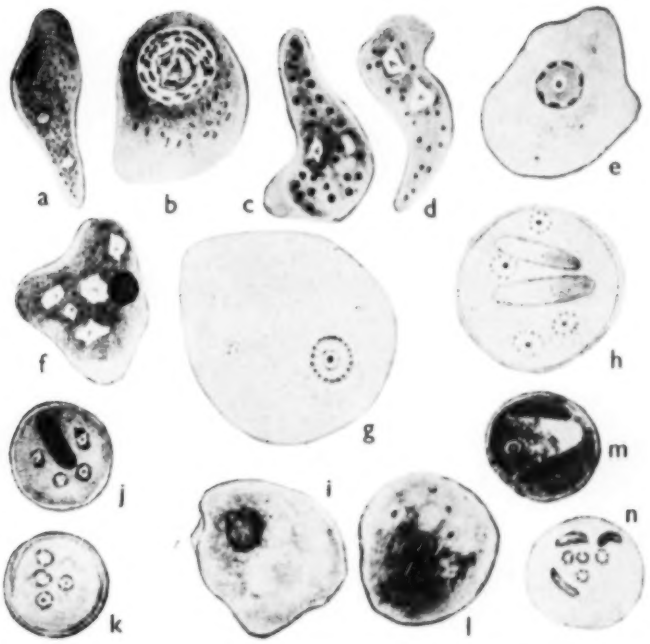

Fig. 2: a—Trophic from of *E. histolytica* as seen in a fresh preparation stained for mitochondria × 1000. b—Same as above. Portion of protoplasm showing the food vacuole, highly magnified. c & d—Trophic form of *E. histolytica* stained supravitally to show Golgi complex × 1000. e—Trophic form of *E. histolytica*, fixed with formalin and stained with methyl green × 1200. f—Trophic form of *E. histolytica* stained with pyronin × 1000. g & h—Trophic and cystic form of *E. histolytica* respectively. Fixed in Zenker's fluid and stained by Feulgen's technique to show the distribution of DNA in the nucleus and the chromatoid bar × 1200. i—Alkaline phosphatase reaction in a trophic form of *E. histolytica* × 1200. j & k—Cysts of *E. histolytica* showing the distribution of alkaline phosphatase × 1000. l—Acid phosphatase reaction in the trophic form of *E. histolytica* × 1200. m & n—Acid phosphatase reaction in the cyst of *E. histolytica* × 1200.

RAY AND SEN GUPTA— *A Cytochemical Study of Entamoeba histolytica* *(pp. 529-33)*

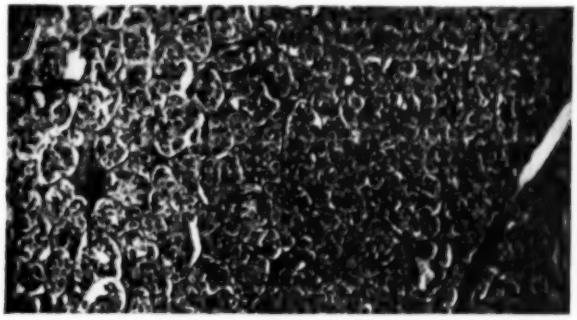

Fig. 1—Islet cell tumour of the pancreas. Microphotograph of specimen removed at operation. Uniform polygonal and large oval cells with no metachromatic staining similar to that of pancreatic acinar cells. Cells are arranged in groups and no ducts were seen. Infrequent mitosis is present but there is no definite malignant change. Differential staining showed the cells to be of beta type.

SUBRAMANIAM AND MENON— *Hyperinsulinism—A Case of Islet Cell Tumour of the Pancreas* *(pp. 537-39)*

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Fig. 1—Photomicrograph illustrates perivascular collar of round cell infiltration. (H & E × 60).

Fig. 2—Photomicrograph illustrates multiple foci of granulomata in the dense connective tissue stroma. (H & E × 60).

Fig. 3—Photomicrograph illustrates oedematous collagenous tissue, marked intimal and medial proliferation of an arteriole occluding the lumen. (H & E × 60).

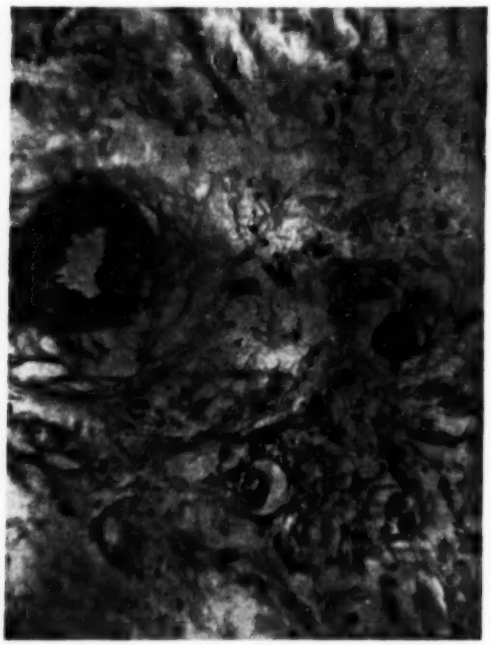

Fig. 4—Photomicrograph illustrates a calcified venule just below the top dead filaria and medial proliferation of an arteriole. Oedematous collagen tissue is seen. (H & E × 60).

others no enzyme could be detected. The chromatoid bars usually gave a faint reaction for alkaline phosphatase. In a tetranucleated cyst, a minute depression resembling a micropyle was seen on the inner aspect of the cyst wall. In close relation to it there were a few granules of cobalt sulphide indicating the presence of the enzyme in this region (Fig. 1, inset). The cyst wall also showed a faint black deposit of cobalt sulphide.

Localisation of acid phosphatase. Smears wet-fixed in chilled aectone were used for the demonstration of acid phosphatase by modified Gomori technique.

The period of incubation in the substrate was usually about 16-20 hours.

Acid phosphatase was seen mainly in the nucleus of the trophic form where granules of lead sulphide were arranged along (? the outer aspect of) the nuclear membrane. The endoplasm also showed relatively faint reaction for the enzyme. The karyosome did not usually give a positive reaction, but a diffuse reaction was often seen in the nucleoplasm Fig. 2, l).

The cysts were found to be rich in acid phosphatase content. The enzyme occurred in the nuclei; the cytoplasm showed granular deposit of lead sulphide and the chromatoid bars showed marked reaction for the enzyme (Fig. 2, m and n).

Demonstration of glycogen. The Bauer-Feulgen method was used for demonstration of glycogen in wet-fixed smears. Saliva-digested controls were used to eliminate the presence of mucin and paraglycogen. After staining with leucobasic fuchsin, the smears were briefly washed in three baths of sulphurous acid instead of metabisulphite; this was regarded as more likely to prevent diffusion artefacts.

Glycogen was present in the endoplasm of the trophic and cystic forms of the amoeba. It was found to occur as hyaline or finely granular mass. In a precystic amoeba, a large hyaline mass of glycogen was seen close to the nucleus. The nucleus and the chromatoid bar did not give any reaction for glycogen.

Demonstration of lipids. Danielli's method for demonstration of free aldehydes which generally form part of a fatty molecule and staining with Sudan IV were adopted for demonstration of lipids in the amoeba.

The fine purple stained granules which could be visualised by Danielli's method were seen to correspond to similar granules stained with Sudan IV. This indicated that these were minute particles of fat distributed throughout the endoplasm of the amoeba.

Discussion

It is proposed to consider the cytological findings of *E. histolytica* in the following order: mitochondria; Golgi complex; other cytoplasmic constituents; and the nucleus.

Mitochondria. Mitochondria are cell organs of definite form in the cytoplasm of cells. They are either filamentous, small rod like or granular structures and are capable of independent motion. These are complex in constitution and are believed to contain several enzymes and vitamins in addition to proteins, glutathione and lipids (Bourne, 1952), and are regarded as store of metabolic material, respiratory enzymes and concerned with digestion of food particles containing proteins, fats and carbohydrates. Wallin (Bourne, (*loc. cit.*) however compared these structures to symbiotic bacteria; but this view is not generally accepted by majority of cytologists. In our preparations of cultures of amoeba stained supravitally, the bacteria present outside the amoeba were not seen to take up the dye, while the elements which we interpret as mitochondria were selectively stained with Janus green. These were small rod shaped or granular bodies moving in the cytoplasmic current of the amoeba. It was thus unlikely that we were confusing mitochondria with bacteria. Besides, dark dot like or small rod shaped structures which were probably the mitochondria could be visualised in the endoplasm of the living amoeba under the phase contrast microscope. In a few specimens aggregation of mitochondria around food vacuoles was seen. Similar appearance was reported in certain amoebae by Horning (Bourne, *loc. cit.*). The change of colour of Janus green to purple, lavender, pink and finally, colourless form is obviously due to oxidation-reduction phenomena in progress in the mitochondria and the cytoplasm of the amoeba. Janus green is known to be reduced first to diethyl saffranine, a pink dye; as oxygen is further consumed the dye is further reduced to a colourless leucobase (Cowdry, 1948). The pink colour in the cytoplasm noted in a few preparations was due to diffusion of the pink dye from the mitochondria; the nucleus was not stained by diffusion. Guillermond and Gautheret (Bourne, *loc. cit.*) however were of the opinion that the change of colour of Janus green inside a cell was not due to simple reduction but to a more complex process.

Regarding the coccobacillary bodies seen in the large food vacuole containing starch grain, it appeared as if these were helping in digestion of starch and the churning movement in the vacuole appeared to be concerned with digestion and absorption of carbohydrate food.

Golgi complex. The Golgi complex possesses the ability to absorb neutral red during supravital staining with this dye. It is variable in structure and shape and is probably connected with some cellular syntheses and acts as a protecting mechanism for the cell against potentially toxic substances which are segregated in it (Bourne, *loc. cit.*).

Golgi complex as already described, could be seen as small spheroidal structures containing the neutral red granules. These are embedded in the endoplasm and move about with the protoplasm of the amoeba. These Golgi spheroids in unstained specimens appear as white vacuoles under the phase contrast microscope. But on supravital staining with neutral red, appear as dark

instead of white and the particles of neutral red are seen inside these structures.

Other cytoplasmic structures—The endoplasm is rich in RNA. Glycogen occurs as hyaline or finely granular masses and fat particles appear as fine granules all through the endoplasm. RNA and glyogen have been found in cysts as well and have similar distribution. The cytoplasm of a fair proportion of cysts and most trophic amoebae often give an impression that these are sprinkled with dust like particles of DNA. The enzyme alkaline phosphatase is present in the endoplasm of the trophic form of the amoeba and the outer border of the ectoplasm producing a bilaminar pattern. The latter pattern is prominently seen in amoebae in smears of sigmoidoscopic specimens or of freshly voided faeces. The intensity of reaction for alkaline phosphatase is less in cultural form of *E. histolytica* than that in its native state in the bowels. This difference is obviously due to variation in the physiological state of the amoeba in the culture media. Acid phosphatase is also present in the endoplasm of the trophic and cystic forms.

There is considerable difference of opinion regarding the validity of localisation of alkaline phosphatase by the Gomori technique and a group of workers led by Novikoff regard the distribution as determined by this method as artefact (Novikoff, 1952). But the arguments advanced by this group have been critically tested by Danielli (1953) and it is at the present time accepted that with short incubation period not exceeding two hours and standardised experimental conditions, modified calcium-cobalt method correctly localises the enzyme. The technique for localisation or acid phosphatase is regarded as less satisfactory and the results 'may be capricious and unreliable'. This technique has not been as critically tested as that for alkaline phosphatase.

In the course of our investigations on the localisation of acid phosphatase, a more or less consistent picture has been obtained of the distribution of this enzyme in the trophic and cystic forms of *E. histolytica*. Though there have been marked variations in the intensity of reaction in both the trophic and the cystic forms, acid phophatase is seen to be localised in the endoplasm.

The distribution of RNA, glycogen and lipids in the cytoplasm of the amoeba does not call for any comment. The presence of fine granules of DNA in the cytoplasm is however an unusual feature. Probably these are concerned with synthesis of proteins, nucleic acids or of the chromatoid bar.

The structure of the chromatoid bar as revealed by this histochemical study is interesting. The chromatoid bars are regarded as store of protein. It has been found that these are made up mainly of nucleic acids, RNA and DNA, the proportion of the two varying with the stage of development of the cysts. The enzyme acid phosphatase is usually present in them and often alkaline phosphatase also. The close association of DNA, RNA and the phosphatases in the chromatoid bars and variation in the relative proportion of DNA and RNA, indicates that active DNA-RNA turnover is in progress in these structures.

Alkaline phosphatase which splits phosphate esters into an alcohol and phosphate reversibiy at a pH optimum of about 9·3 is recognised to be of great importance in the life process of cells. According to Danielli, the phosphatase usually represents the enzymic centre of a contractile protein and it is concerned among other processes with nucleic acid and protein synthesis. The enzyme is also responsible for phosphorylation and dephosphorylation that are necessary for absorption or secretion of substances into or out of cells.

The layer of phosphatase on the outer border of the ectoplasm is probably concerned with transfer of soluble food material, e.g., glucose, amino acids, etc., from outside into the amoeba and excretion of the end products of metabolism. This layer thus appears to be the selectively active border of the amoeba. The enzyme in the endoplasm is concerned with the metabolic processes that are referred to above. From the distribution of the enzyme in a tetranucleate cyst (*vide supra*) it appears probable that alkaline phosphatase is in some way related to excystation of the amoeba.

The nucleus—The nucleus of *E. histolytica* contains a very small quantity of DNA. Both with the Feulgen reaction and staining with methyl green, DNA could be seen to stain very delicately and finely. (Localisation of Feulgen-positive granules in the amoeba was facilitated by phase contrast microscopy). The DNA containing structures appear much smaller than nuclear chromatinic material of the amoeba stained by iron haematoxylin.

The nucleoplasm contains RNA and the nuclear membrane is made up of the same material. Alkaline phosphatase is present in the nuclear membrane and usually in the karyosome and the nucleoplasm often shows faint to moderate reaction for the enzyme. The distribution of alkaline phosphatase in the nuclear membrane is similar to that of DNA, though the pattern produced by cobalt sulphide granules is very much coarser. The intense reaction for the enzyme in the chromosomes of the amoeba and the faint reaction in the mitotic spindle are in keeping with the experience of other workers with different cells (Danielli, *loc. cit.*).

It may be added that at least three possible functions are ascribed to nuclear phosphatase, *viz.*, protection of genes against a number of vigorous phosphorylating agents such as adenosine triphosphate and acetyl phosphate; mediation of final stage of gene formation and nucleic acid synthesis (Danielli, *loc. cit.*).

The distribution of acid phosphatase in the amoeba as obtained by us has been described. But in view of the prevailing uncertainty about the validity of localisation of this enzyme by lead phosphate method, the results are presented without any comment.

Summary

The results of cytochemical study of trophic and cystic forms of *E. histolytica* for the presence of mitochondria, Golgi complex, nucleic acids, phosphatases, glycogen and lipids are presented.

It has been found that mitochondria are present in the endoplasm of the trophic form and that they exhibit oxidation-reduction phenomena. The Golgi complex is present in the endoplasm and is spheroidal in structure.

The amoeba is rich in RNA and contains relatively minute amounts DNA in the nucleus. Its cytoplasm both in the trophic and cystic forms, gives an impression of the presence of minute dust like particles of DNA scattered all over the endoplasm.

The chromatoid bars are made up mainly of RNA and DNA and contain the phosphatases. There is evidence suggestive of active DNA-RNA turnover taking place in these structures.

Alkaline phosphatase is present in the nuclear membrane and the karyosome and less frequently in the nucleoplasm of the amoeba and it is also present in the endoplasm and in the outer border of the ectoplasm at times exhibiting a bilaminar pattern. The cysts show a positive reaction for alkaline phosphatase in the nucleus and a variable reaction in the cytoplasm.

Acid phosphatase is present in the nucleus along the nuclear membrane and often the nucleoplasm; endoplasm also shows a weaker reaction. The cysts show positive reaction for this enzyme both in the nucleus and the endoplasm. The chromatoid bars show marked reaction for phosphatase.

Glycogen is present in the endoplasm of the trophic and cystic forms of the amoeba. Minute particles of lipids are distributed throughout the endoplasm of the trophic form of *E. histolytica*.

The significance of the findings has been discussed.

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CANCER OF THE TONSIL

(Observations on 152 Cases)

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It seems from the available literature that cancer of the tonsil is not so frequent as we meet in our hospital. Moreover, the consensus of opinion is that the result in therapy of cancer tonsil is poor and the prognosis is poorer. This communication is an attempt to discuss the pathological aspect of cancer tonsil as manifested by one hundred and fifty-two cases who were seen in the out patients' department or admitted to the Chittaranjan Cancer Hospital, Calcutta, within the period of four years since the inception of the Hospital in 1950 to the year 1953 inclusive. Here the word cancer has been used as a general term which includes all kinds of malignant tumours.

Materials and Methods

The materials were received from the otorhinolaryngology service of Chittaranjan Cancer Hospital, Calcutta.

The methods of identification or diagnosis were clinical findings, biopsy and cytopathological examination after Papanicolau's technique. Kahn's flocculation test was done as a routine pocedure. Skiagrams of chests were studied for secondary involvement of the mediastinum, lung and pleural cavity. No autopsy examination was available on any of these types of patients, so a valuable portion of observation goes without record. No attempt has been made to evaluate the correlationship of pathology with therapeutic results in this communication.

Observations

Incidence—During the four year period, 1950 to 1953 inclusive, there have been 5,071 patients with primary malignant tumours attending the Chittaranjan Cancer Hospital, Calcutta. Of this group there were 1,388 cases of neoplasms of ear, nose and throat region i.e. 10·96 per cent of all malignant neoplasms seen in the hospital. Among these there were 152 instances of malignant tumours in the region of the tonsil. Thus cancer of the tonsil constitute 2·99 per cent of all cases of cancer who attended the hospital. It is evident from Table 1 that this comprises 1 to 3 per cent of all kinds of cancer. This fact corroborates the figure (1·5 to 3 per cent) given by Parshall and Stenstrom (1952). The total number of malignant tumours of the pharynx was 303 and so the tonsil cases amongst the pharynx cases came out to be 50·2 per cent (Fig. 1). Teloh (1952) found tonsillar tumour to be 22·2 per cent of all pharyngeal cancer cases in his series.

TABLE 1—SHOWING INCIDENCE OF CANCER TONSIL IN ALL MALIGNANT LESIONS

	% among all malignant lesions
Pack and LeFever (Memorial Hospital, N.Y.C.) ...	2·23
Schall (Huntington Memorial Hospital, N.Y.) ...	0·94
Teloh (Pondiville Hospital, Mass.) ...	1·2
Dutta-Chaudhuri & Roy (Chittaranjan Cancer Hospital, Calcutta)	2·99

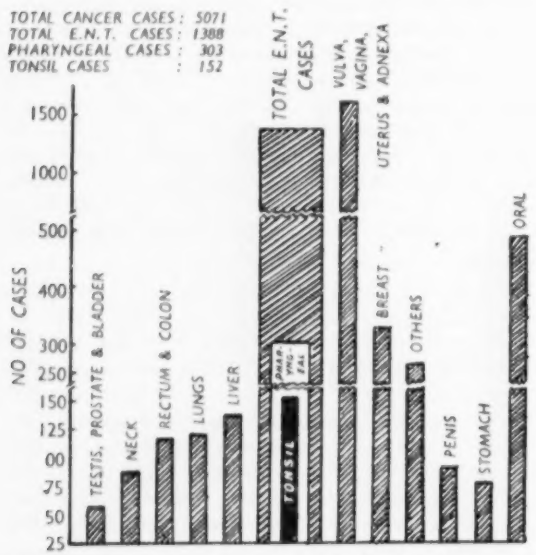


FIG. 1—SHOWING THE INCIDENCE OF PRIMARY MALIGNANT TUMOURS IN CHITTARANJAN CANCER HOSPITAL, CALCUTTA, 1950-53

Age Incidence—The age incidence of cancer of the tonsil as was met in this series is presented in Table 2. The youngest patient was aged 28 years and the oldest 81 years. Higher peak was observed in cases of 35 years to 69 years of age, the highest peak being at 45 to 64 years. The peak incidence of Teloh's series (1952) was at 65 to 69 years, the extremes were a child 3 years old and a man of 87 years. Average age of tonsillar carcinoma in Duffy's series (1932) was 55·4 years, the extreme ages being 21 years and 78 years. Burnam's series (1932) had relatively early age incidence, the commonest being at 40 years of age. We agree with Willis (1953) that lymphoepithelioma type occurs earlier than the other types. In our series of three, the ages were 46 years, 54 years and 45 years.

TABLE 2—SHOWING AGE INCIDENCE

Years	*Male*	*Female*	*Total cases*
Below 30	2	–	2
30—34	2	–	2
35—39	7	4	11
40—44	8	2	10
45—49	23	2	25
50—54	27	4	31
55—59	14	4	18
60—64	24	6	30
65—69	8	3	11
70—74	6	–	6
75—79	1	3	4
80—81	2	–	2

Youngest 28 years **Oldest 81 years.**

Sex Incidence—The incidence of epidermoid and squamous cell types of carcinoma is high in males. In our series histologically typed cases were 127. Among these, 119 were epidermoid type and squamous type together. Among these 119 cases, 101 occurred in males with incidence of 84·9 per cent. Teloh (*loc. cit.*) reported 98·6 per cent in males, Walker and Schulze (1947) 84 per cent, Martin and Sugarbaker (1941) 86 per cent, Mattick (1940) 91·3 per cent, Schall (1934) 88·7 per cent, Burnam (*loc. cit.*) 77·5 per cent, Desponse (1928) 92 per cent and Nathanson (1928) 95 per cent.

But this kind of sex predominance was not seen with other types of lesions. The case of plasmocytoma, two out of three cases of lymphosarcoma, two out of three cases of lymphoepithelioma and the case of Hodgkin's sarcoma occurred in females. In Teloh's (*loc. cit.*) series also 12 out of 21 cases of lymphomas occurred in females. Though no conclusion can be drawn from this small number of cases, it seems that non-epithelial group of tumours are more common in females while the epithelial groups are common in males.

Religion—One hundred and twenty cases (78·9 per cent) occurred among Hindus, twenty-eight cases (18·5 per cent) among Muslims and four cases (2·6 per cent) among Christians. This difference in incidence might be due to the fact tht the majority of our hospital population were Hindus.

Habits—Habits of chewing betelnuts with or without *jarda, kimam, docta* (these are tobacco preparations) and dried tobacco leaf and that of smoking were investigated. The observation shows maximum lesion to have occurred in the tonsil of smokers, 76 in 107 i.e. 71 per cent (Table 3).

TABLE 3—SHOWING SPECIAL HABITS OF THE PATIENTS

	Habits	*No. of cases*
1.	Pan (betel leaf)	12
2.	Pan, jarda and dry tobacco leaf ...	11
3.	*Smoking	37
4.	Pan and *smoking	33
5.	Pan, jarda, dry tobacco leaf and *smoking ...	6
6.	No such habits	8

Total no. of smokers: 76 No record available: 45

Site Incidence—None of the cases in this series got bilateral affection. Eighty-one out of one hundred and fifty-two cases had right-sided lesion. Duffy's (*loc. cit.*) series had left-sided lesion in sixty-nine out of one hundred and twenty-one cases. So it seems that there is no predilection for any side.

Symptoms—Symptoms and signs as observed, are shown in Table 4. Majority of cases in this series had advanced disease condition, when admitted into the hospital. Pain and difficulty in swallowing were the most common signs occurring in 118 cases (77·6 per cent), and next in order the lump in the neck, 31 cases (20·4 per cent). Pain in the ear was also an early

TABLE 4—SHOWING SYMPTOMS OF CANCER OF THE TONSIL

	Symptoms	*No. of cases*	%
1.	Pain and difficulty in swallowing ...	118	77·6
2.	Lump in the neck	31	20·4
3.	Pain in the ear	27	17·8
4.	Change in voice	23	15·1
5.	Pain in the throat	22	14·5
6.	Salivation	9	5·9
7.	Bleeding	6	4·0
8.	Sore throat	9	5·9
9.	Pain in the temporal region and headache	3	2·0

symptom in 27 cases (17·8 per cent). In some series sore throat was the predominating early symptom—Walker and Schulze (*loc. cit.*) 54 per cent, Teloh (*loc. cit.*) 40·4 per cent. Sore throat seems to be infrequent in our series, 9 cases (5·9 per cent) only.

Duration of Symptoms before coming to Hospital—The duration of symptoms in pre-hospitalisation period is as follows: Fifty-five cases (38·7 per cent) had history of less than three months; forty-eight cases (33·8 per cent) less than six months; twenty-one cases (14·8 per cent) less than one year; fourteen cases (9·9 per cent) less than two years; and four years (2·8 per cent) had history of less than three years. Ten patients could not give any definite history.

Macroscopic Characters of Lesions—The cases in the series under review can be divided into five groups: 1. Proliferative 20 cases (13·2 per cent). 2. Ulcerative 30 cases (19·7 per cent). 3. Infiltrative 45 cases (29·6 per cent). 4. Ulceroproliferative 40 cases (26·3 per cent). 5. Smooth growth 17 cases (11·2 per cent).

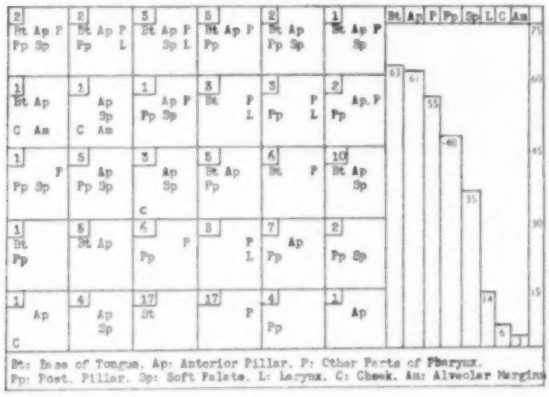

Bt Ap P Pp Sp L C Am
Bt: Base of Tongue. Ap: Anterior Pillar. P: Other Parts of Pharynx.
Pp: Post. Pillar. Sp: Soft Palate. L: Larynx. C: Cheek. Am: Alveolar Margins

FIG. 2—SHOWING INVOLVEMENT OF THE STRUCTURES ADJACENT TO THE TONSIL

Fig. 2 shows that only twenty-eight cases had lesions limited to tonsil (18·4 per cent) and twelve cases limited to tonsil and one of the two pillars or both the pillars. The rest of the cases had involvement of the other surrounding structures. Among the surrounding structures, base of the tongue was involved in 63 cases (41·4 per cent), anterior pillar 61 cases (40·1 per cent), other parts of the pharynx 55 cases (36·1 per cent), posterior pillar 48 cases (31·6 cases), soft palate 35 cases (23 per cent), larynx 14 cases (9·2 per cent), cheek 6 cases (3·9 per cent) and alveolar margin 3 cases (1·95 per cent). One of the cases of basal cell type of epidermoid carcinoma involving the cheek, involved angle and ramus of the mandible two years after the first visit though treated with roentgen therapy, as evidenced by skiagraphy.

It will thus appear from the above findings that forty cases (26·3 per cent), at least, are primary lesions and the rest might have their primary in tonsil or in any of the surrounding structures.

Incidence of Lymphadenopathy—Cervical lymphadenopathy was present in one hundred and twenty-six cases (82·8 per cent) of which ninety-four (74·6 per cent) was unilateral. The incidence of lymphadenopathy in the series of Teloh (*loc. cit.*) was 75·7 per cent, Schall (*loc. cit.*) 92 per cent, Mattick (*loc. cit.*) 77·3 per cent, Martin and Sugarbaker (*loc. cit.*) 76 per cent, and Burnam (*loc. cit.*) 70·3 per cent. Lymphadenopathy on the first day of attendance has only been considered.

Histological Observation—A review of sections done from biopsy material obtained from one hundred and twenty-seven cases is presented in Table 5. Among the remaining twenty-five, thirteen cases were biopsy negative but smear positive. Biopsy was not done in twelve cases on clinical grounds, some of them however, were smear positive. The smear technique and results have been discussed elaborately by Dutta-Chaudhuri *et al* (1954).

TABLE 5—SHOWING HISTOLOGICAL CLASSIFICATION OF MALIGNANT LESIONS

	Type	*Male*	*Female*	*Total*	%
1.	*Epidermoid Carcinoma	77	14	91	71·7
	(a) Transitional Type	61	8	69	54·3
	(b) Spindle Cell Type *	2	1	3	2·4
	(c) Basal Cell Type	3	—	3	2·4
	(d) Small Cell Type	3	2	5	3·9
	(e) Anaplastic Type	3	1	4	3·2
	(f) Ungraded	5	2	7	5·5
2.	*Squamous (Spinal) Cell Type	24	4	28	22·1
3.	*Lymphoepithelioma	1	1	3	2·4
4.	Lymphosarcoma	1	2	3	2·4
5.	Plasmocytoma	—	1	1	0·8
6.	Hodgkin's Sarcoma	—	1	1	0·8

*Epid. Ca + Sq. Cell Ca = 119 i.e. 93·7%
*Epid. Ca + Sq. Cell Ca + Lymphoepithelioma = 122, i.e. 96·1%

Table 5 shows that majority of the cases were of epithelial origin which includes epidermoid carcinoma, squamous cell carcinoma and lymphoepithelioma

(Schimke and Regaud) the number being 122 cases out of 127 i.e. 96·1 per cent. Three cases were found to be lymphosarcoma and one case each of plasmocytoma and Hodgkin's sarcoma.

Other workers have observed giant follicular lymphoma (Baggenstos and Heck, 1940; Mayer, 1948) and adenoid cystic carcinoma (Pack and LeFaver, 1930), we had no such cases in our series.

Burnam (*loc. cit.*) reported secondary deposit in tonsil in three cases, two from the breast and one from testis. We did not meet any such cases.

Further details of histology have been worked out. That will be dealt with in another communication. But it may be mentioned here that the sub-groups of epidermoid carcinoma (Table 5) as is done here seems to have a clinical bearing.

Correlation between the Histologic Type and Macroscopic Appearance of Lesion

Epidermoid and squamous cell carcinoma group shows all macroscopic varieties as described above but one characteristic point is that they have got induration or hard edge on digital examination whether early or late, ulcerated or not. The lower pole of the tonsil is involved in most of these lesions (125 in 144 cases). Others involved the whole of the tonsil.

Lymphoepithelioma group shows an enlargement of the tonsil three to eight times of its normal size and they are invariably accompanied by lump in the neck, very often upto the size of a grape fruit.

Among the three cases of lymphosarcoma two had round fleshy mass involving the tonsil with small palpable lymph nodes in the neck. The third had an ulcerative growth and had generalized lymphadenopathy with enlarged spleen and fluid in abdomen in the later stage.

The case of plasmocytoma had the smooth tonsillar growth of the size of a lemon with infiltration into the surrounding structures and bilateral lymphadenopathy in neck.

The Hodgkin's sarcoma case had nothing of its own characteristics to differentiate from others.

Discussion

Before going into the discussion let us analyse the normal structure and character of the tonsil. The tonsils are compound aggregates of lymphatic nodules, encapsulated in dense fibrous connective tissue which is continuous with that of the pharyngeal submucosa. The tonsillar surface is covered with stratified squamous epithelium invaginated into the subjacent lymphatic tissue to form crypts of varying depths. The integrity of the lining epithelium is most often broken at the depth of the tonsillar crypts. Invasion of the epithelium by lymphocytes and escape of lymphocytes into the crypts are important features of the tonsil. Tonsils lack afferent lymphatic vessels but they have efferent vessels.

From the above it is evident that the malignant tumour may have its origin from any of the component tissues—epithelium, connective tissue, lymphoid tissue and blood vessels; but curiously enough epithelial tissue seems to be more active in giving rise to carcinoma which is 96·1 per cent in our series.

There is no tumour which might have its origin from connective tissue and blood vessels. No reference also could be found out in literature to that effect. Among the other tonsillar growths the lymphoid tissue takes the predominant role as it gives rise to giant follicular lymphoma, lymphosarcoma, Hodgkin's disease and plasmocytoma. The origin of plasmocytoma from the lymphoid tissue adds to the evidence that plasmocytes are of lymphatic origin.

The characteristic lymphatic vascular system gives an explanation why secondary deposit from distant organ is so rare in the tonsil and lymphadenopathy particularly of neck is so common. Sometimes it is the neck lymphadenopathy which compels this group of patients to consult the family physician.

Etiology

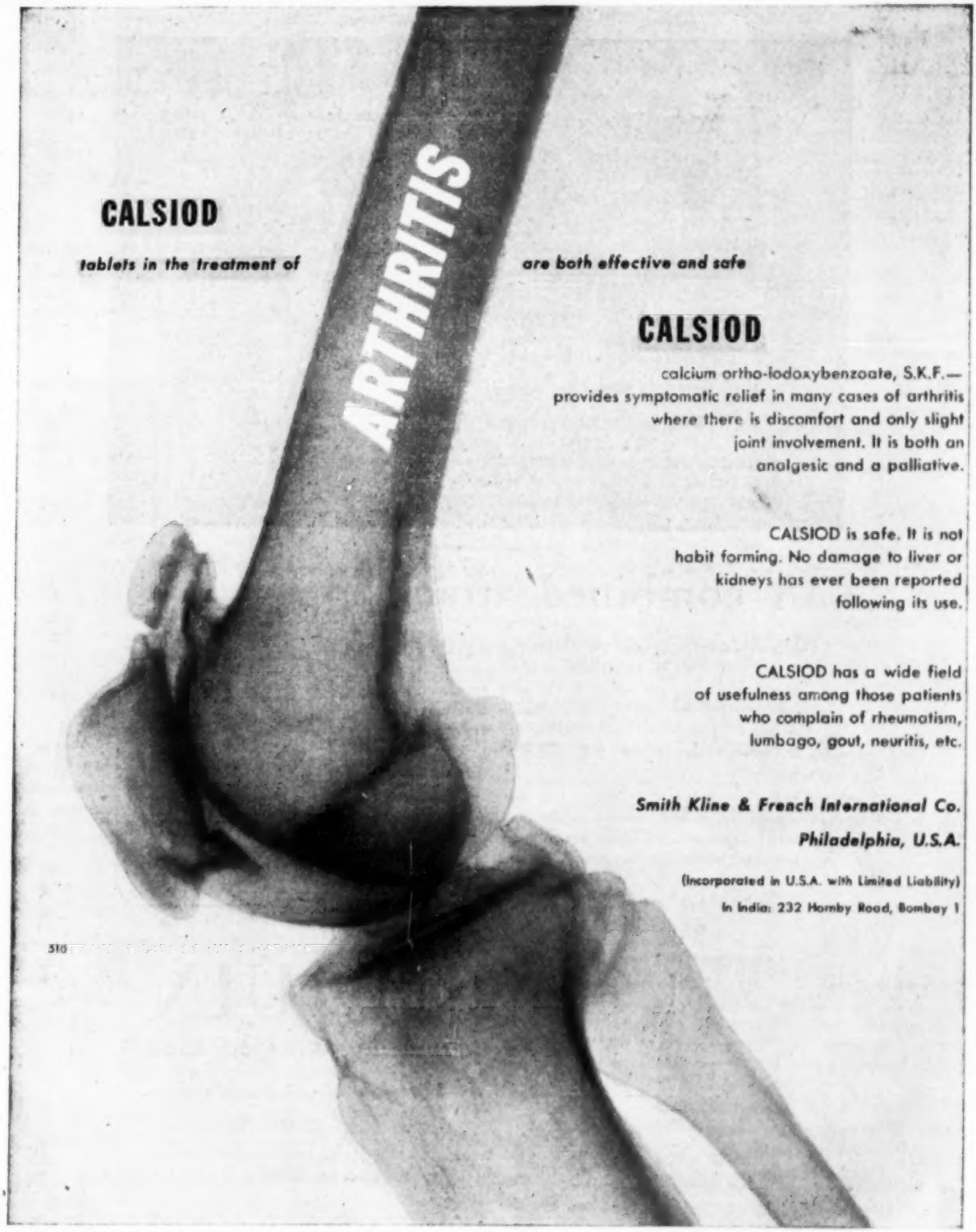
Tonsil itself presents certain structural weakness in the epithelial lining covering the lower ramifications of their crypts where they become very much thinned and at certain parts deficient. This thinning of covering tissue helps the bacteria to penetrate the underlying tonsillar tissue. Repeated attacks by bacteria causing repeated inflammation may help in producing the fell disease as chronic inflammatory conditions act as predisposing factors in carcinoma of cervix uteri.

In our investigation it is evident that smokers are more vulnerable (71 per cent) to this disease. Bloomfield (1920) found that carbon particles in the mouth tend to remain longer upon the mucous membrane in the tonsillar region than in other parts of the buccal cavity, so the smoke carrying any carcinogenic substance or soot may be deposited in the tonsil and act as a carcinogen. This kind of fact is advocated in case of bronchogenic carcinoma, so why will not the same fact act here? Kahn test was positive in seven cases out of one hundred and fifty-two, so it can be held that syphilis does not play any etiologic role.

Betelnut does not seem to play any part as an etiological factor as evidenced by our observation (Table 3).

Diagnosis

It is evident from this series of 152 cases that 12 had their treatment without any diagnosis by biopsy and another 13 cases had negative biopsy report. Most of the cases of both these groups showed positive in smear and rest were proved by roentgen therapy in the line of malignancy. These facts go to prove that it is very difficult to choose the proper place in the tonsil for



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biopsy examination. Moreover, there are certain types of lesions, e.g., anaplastic group of carcinoma which require prebiopsy radiation because this procedure of biopsy may result in dissemination of the growth. Post-radiation biopsy usually does not give proper result. So Dutta-Choudhuri *et al* (1954) advocate the smear technique of diagnosis in those cases. They reported 96·78 per cent accuracy in ear, nose and throat cases.

ACKNOWLEDGMENT

We take this opportunity to thank Dr. Subodh Mitra, Director, Chittaranjan Cancer Hospital for his kind permission to publish this paper. Our thanks are also due to Dr. B. Sen Gupta, Visiting Surgeon and to Dr. S. Roy, Consulting Surgeon to Otorhinolaryngology Service of Chittaranjan Cancer Hospital for helpful criticism.

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HYPERINSULINISM—A CASE OF ISLET CELL TUMOUR OF THE PANCREAS

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The first case of hypoglycaemia due to an islet cell tumour (carcinoma) of the pancreas was described by Wilder and others (1927) with operative and necropsy findings from the Mayo Clinic. This patient had metastases in the liver from which potent insulin was obtained. Nicholls (1902) found an adenoma of the islets at autopsy and Warren (1926) had twenty such cases, but no clinical significance was attached until Harris (1924) described the syndrome of hyperinsulinism and Wilder (*loc. cit.*) published his case in 1927. Howland and others (1929) reported the first cure of a patient by surgical removal of a tumour of the islet cells of the pancreas. Since then it has been found that the incidence is far from uncommon and the literature on the subject has become voluminous.

We have here described a case successfully treated by surgery, with no evidence of metastases elsewhere.

CASE REPORT

Patient S., aged 38 years, Hindu, male, was admitted into the Government General Hospital medical wards on 6-5-52 in a semiconscious state. History, as obtained from the relatives revealed that the patient was subject to attacks of unconsciousness for the previous two years. It first started when he was bathing in a river and was almost drowned; two hours after rescue he regained consciousness. Since this incident he often used to get "attacks" which were characterised by general weakness, followed by dimness of vision, later merging into a deep sleep; occasionally they were accompanied by convulsions. Just prior to admission these attacks became more frequent and of longer duration. Previous to this trouble, the patient was being treated by hypertension; there was no evidence in the history of his having contracted any venereal infection.

Clinical examination revealed a malnourished, anaemic individual of about 35 years, in a semi-conscious state, with twitchings of the right corner of the mouth, and profuse sweating. No convulsions were observed. Both pupils were equal, central, regular, dilated, immobile. All reflexes were absent except for the plantar which was extensor on the right side. The bladder was slightly distended. The patient was able to appreciate pin-prick and pressure pain.

The cardiovascular, respiratory, and alimentary system did not show any abnormality.

The following investigations were carried out immediately:

Urine—Reaction, acid; specific gravity, 1015; albumin and sugar, absent. Bile salts and bile pigments absent.

Blood: R.B.C.—2·5 million/c.mm. Hb.—50 per cent; W.B.C.—4000/c.mm. with polymorphs 60 per cent, lymphocytes 28 per cent, monocytes 3 per cent and eosinophils 7 per cent.

Lumbar puncture: C.S.F.—tension normal; colour clear. Quickenstedt pressure conducted; 3 cells/c.mm. Biochemical analysis of cerebrospinal fluid showed: proteins—20 mg. per cent; globulin—nil, chloride—700 mg. per cent and sugar—too low for estimation. No organisms could be grown in culture.

Immediate stimulant therapy was adopted. Glucose was administered intravenously and coramine was given parenterally every four hours. The patient recovered consciousness in about an hour's time.

Subsequent re-examination revealed the following:

Intelligence was normal but memory poor. Cranial nerves were all normal. Except for brisk ankle jerks and doubtful extensor plantar on both sides, nothing abnormal was detected. Micturition disturbances occurred only when the patient became stuporous during the periods of loss of consciousness. He was not able to say if anything in particular provoked the attacks.

During his stay in the wards it was observed that the patient used to get convulsions or pass into a stuporous or semi-conscious state in the early hours of the morning or when his meals were delayed. Administration of glucose immediately restored him. These facts and the negative results of the previous investigations suggested a diagnosis of hypoglycaemia and the following tests were therefore carried out:

Random blood sugar—37 mg. per cent.

Blood sugar after administration of adrenaline—90 mg. per cent.

Glucose tolerance test (Fig. 2).

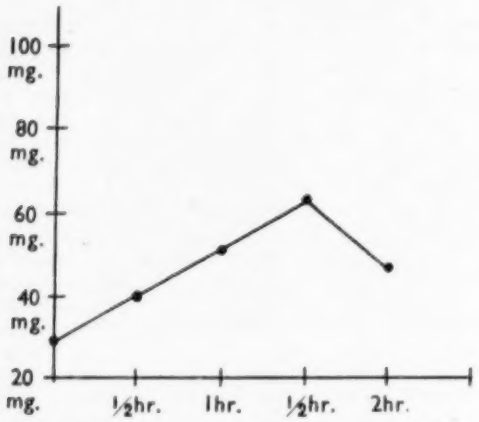

FIG. 2—PREOPERATIVE GLUCOSE TOLERANCE CURVE

Liver function tests—normal.

Serum proteins: Total—7·2 g. per cent; albumin 3·0 g. per cent and globulin 4·2 g. per cent.

Blood cholesterol—261·4 mg. per cent.

Having eliminated liver diseases (from above results), and hypoadrenalism from blood pressure studies, a tentative diagnosis of hyperinsulinism was made. An exploratory laparotomy was therefore decided upon in collaboration with the surgeon to confirm the diagnosis and assess the line of treatment.

Operation notes—On 26-5-52, under general anaesthesia the abdomen was opened by a right paramedian incision. The stomach, duodenum, small intestine and liver were found to be normal. The lesser sac was opened up by dividing the gastrocolic omentum and the anterior surface of the pancreas was exposed. A small localised tumour was found protruding from its surface near the middle of the body of the gland. It was roughly globular, lobulated and soft in consistency. The tumour was shelled out easily by blunt dissection. The true capsule was found. No other nodules or tumours were felt or found in or near the pancreas. The raw area was closed by catgut sutures, and the abdomen was closed in layers.

Pathological report—The whole tumour consisted of islet cells, arranged in groups, and no ducts were seen. Infrequent mitosis is present, but there is no definite malignant change. Differential staining showed the cells to be of the beta type. (Fig. 1, *vide* Plate).

Progress: Post operative convalescence was uneventful. The attacks never recurred (one year follow up was done).

The glucose tolerance test (Fig. 3) and serum protein determination were repeated. Serum proteins: Total proteins—6·8 g. per cent; albumin—4·0 g. per cent and globulin 2·8 g. per cent.

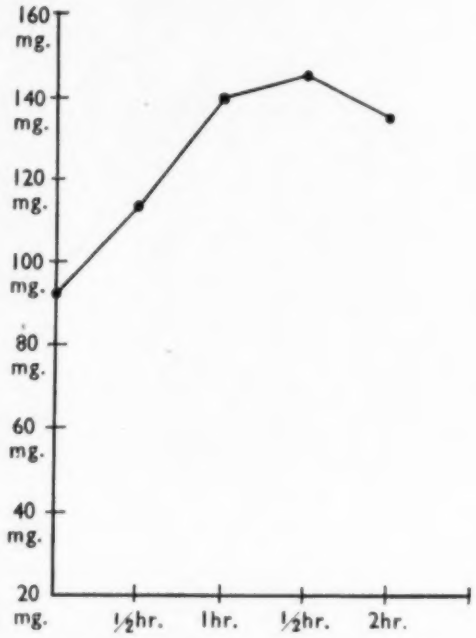

FIG. 3—POSTOPERATIVE GLUCOSE TOLERANCE CURVE

DISCUSSION

Hyperinsulinism is a condition in which there is excessive secretion by the islet cells of the pancreas resulting in spontaneous hypoglycaemia, the symptoms resembling those due to an overdose of insulin. The condition can exist without a tumour, and is then said to be due to hyperplasia of the islet cells, but in its most definite form, it is seen in cases possessing an islet cell tumour. In the differential diagnosis, however, one must consider diseases of the liver affecting glycogen storage, hypofunctioning of other endocrine organs like the adrenal, thyroid and pituitary, and surreptitious self-administration of insulin. Whenever fasting results in symptoms of marked hypoglycaemia with blood sugar values below 50 mg. per cent, the presence of an islet cell tumour must be presumed (after exclusion of extrapancreatic causes mentioned above), unless otherwise proved. In the present case there was no evidence clinically of hypoadrenalism and the 17-ketosteroid estimation was not therefore done. The basal metabolic rate was not done because the patient could not starve long enough. This may be explained by the damage incurred by the liver due to the prolonged hypoglycaemic state. The subsequent return to normal will justify this statement, for if liver damage

is sufficiently advanced to produce such hypoglycaemia, changes are likely to be irreversible.

It is commonly stated that most adenomata occur in the tail and body of the pancreas, since islet tissue is most abundant in the tail. Among 254 functioning adenomata analysed by Howard, Moss and Rhoads (1950) the location of the tumours was as follows: head 66; junction of head and body 10; junction of body and tail 25; tail 84; ectopic 7. Aberrant locations have chiefly been in the duodenal wall around the hiatus of the spleen and posterior to the pancreas. Theoretically adenomas may be in any area where ectopic pancreatic tissue is found, such as in Meckel's diverticulum in the wall of the gall bladder and in the wall of the stomach. The incidence of multiple tumours is sufficiently great (10-12 per cent) to make it an important duty of any surgeon to make sure at the operation that no more than one nodule can be seen or palpated. In the case by Maxeiner and Bundy (1945) 75 per cent of the pancreas was removed and it was found to contain 8 small islet cell tumours. Most of the reported adenomas have varied from 1-2 cm. in diameter, and some of the functioning tumours may be only 2·5 mm. in diameter. They are usually grossly pink or yellowish pink in colour, and firmer than the surrounding pancreatic tissue. The tumours are highly vascular and the capsule of the tumour is usually incomplete. Histologically, it is difficult to differentiate between malignant and benign islet cell tumors.

In the diagnosis no elaborate diagnostic procedures are necessary. The characteristic symptoms associated with well marked hypoglycaemia brought on by fasting, increased by physical exertion, relieved by food are the important features. The glucose tolerance test is of value only if carried out for a sufficient length of time, i.e., for four, five, or six hours. Up to the third hour, it may be normal or mildly diabetic in type except for the initial low level. After three hours the blood sugar usually falls sharply to a low level, and in the fifth and sixth hours shows no tendency to rise spontaneously towards normal (unlike the normal individual where a hypoglycaemia phase in the glucose tolerance curve is often obtained but returns to normal again due to the secretion of epinephrine). Various secondary tests may be carried out including blood sugar studies following the administration of epinephrine, pituitary extracts, ergotamine and insulin. The blood sugar findings are usually very low—below 50 mg. per cent, although it has been observed that the blood sugar should be low for the patient and not as judged by any other standard.

Once the diagnosis of islet cell tumour is made, surgical treatment is indicated, because complete cure is expected, and medical treatment is unsatisfactory. Delay in surgery with continuance of the hypoglycaemic attacks may cause irreparable damage to the central nervous system, and further, the possibility of a malignant change occurring in the adenoma is present.

In certain instances where the clinical findings are vague and blood sugar values are not constantly and definitely below normal, and when exploration fails to reveal a tumour, non-surgical treatment can be tried. In the acute attacks administration of carbohydrate in easily assimilable form is the best treatment. In the prevention of attacks, a diet low in carbohydrate and high in protein has been found to be most useful. Drugs are not of much value in the prevention of hypoglycaemic attacks. For short periods the administration of ACTH might be considered. Theoretically, at least, alloxan might be of value in the treatment of hyperinsulinism. Since physical activity accentuates the tendency to hypoglycaemia exercise must be taken with moderation.

The incidence of functioning islet cell tumours resulting in hypoglycaemia is not at all uncommon, but the diagnosis of the same is important because complete cure is possible, and timely surgery is essential to prevent permanent damage to the central nervous system. The condition is receieving the desired recognition, and should be in the minds of all practitioners when confronted with obscure cases of coma or convulsions.

ACKNOWLEDGMENT

We are greatly indebted to our colleague Dr. M. Krishnamurthy, Surgeon, and to Dr. D. Govinda Reddy, Pathologist, for collaboration and to Dr. C. K. Prasada Rao, Dean, Government General Hospital, Madras, for kind permission to publish this case.

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MODIFIED KONDOLEON'S OPERATION FOR ELEPHANTOID LEGS

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Surgical treatment of 50 cases of elephantoid legs due to filarial infestation, was undertaken during the last 2½ years at the Government Hospital, Rajahmundry. This town and the neighbouring districts are highly endemic spots for filariasis and several adults are incapacitated from earning their livelihood in consequence. The clinical recognition of these cases is easy, although microfilaria were rarely found in the blood of the patients treated.

Morbid Anatomy and Histology of the Excised Tissues

The skin was excessively hard, thickened, fissured and nodular. Papillary acanthosis, marked hyperkeratosis and thickened fibrotic dermis with numerous foci of round cell infiltration were the chief histological findings. The corium was composed of abundant oedematous fibrous tissue, some of which was of collagen type. Multiple foci of round and plasma cells, with an occasional foreign body giant cell, were seen throughout the dermis. Perivascular collections of round cells in the form of a collar, with or without endarteritic changes, partially occluding the lumen of the vessel were observed. (Figs. 1 and 2, *vide* Plate). Inflammation of the intima of the vessels and total occlusion of the lumen by calcified dead microfilaria were occasionally encountered (Figs. 3 and 4, *vide* Plate). Lymphangiectasis and hypertrophy of the musculature of the vessel wall were observed.

The serous fluid that exuded during excision of the elephantoid tissues contained 3·5 grammes per cent of proteins and 640 mg. per cent of chlorides. Staphylococci were recovered from cultures of the excised tissue and questionable criminality could be attributed to them for the elephantoid condition.

Anatomical Basis of Kondoleon's Operation and the Need for its Modification

Very few seem to have practised the operation described by Kondoleon of Greece in 1912 for the surgical treatment of elephantoid legs. The operation has been modified by the present author and has since been adapted by him as the standard surgical procedure for elephantoid legs.

As early as 1874 Sappey observed that the deep fascia forms an impenetrable barrier for the exchange of lymph between the superficial and the deep lymphatic systems in elephantoid states. Kondoleon (1912) clinically confirmed Sappey's observation, in that the thickening in elephantiasis is confined to tissues superficial to the deep fascia. Abundant proliferation of fibrous and collagenous tissue as a result of lymphatic or venous obstruction induced either by the filaria blocking the lumina or due to bacterial phlebitis, impede the free exchange of lymph. Excessive formation of collagen tissue produced by simultaneous venous and lymphatic obstruction is clinically recognised by the non-pitting type of oedema that is observed in elephantoid states. Great increase in lymph flow is often produced by ligaturing the main vein of the limb, establishing the intimate relationship of the veins and lymphatics. Embryologically, lymphatics are offshoots of the veins and naturally may be related functionally too.

Kondoleon excised long strips of subcutaneous tissue and deep fascia and sutured the wound, and established intimate contact between the subcutaneous tissues and the muscles with the object of draining the lymph from superficial zones into the inter and intramuscular lymphatics. Excision of strips of deep fascia was carried out as outlined by Kondoleon in a few of the 50 cases operated on. Very little reduction in size of the limb and the poor cosmetic effects resulting from the operation compelled me to modify the original Kondoleon technique. In the second series of cases, by elliptical flaps, large masses of elephantoid tissue were excised down to deep fascia under the dissected flaps. Incisions were planned at times to include elephantoid nodules for excision along with strips of deep fascia. The flaps were drawn together by under cutting the skin. The excision used to be done in three stages, excision of the posterolateral aspect at the first sitting, excision of the medial aspect at the second sitting and the operation completed at the third sitting by excising the foreign tissue over the dorsum of foot. The operation having to be completed in three stages, with the attendant prolonged hospitalisation and the not very encouraging results from the cosmetic point of view, made me improve the Kondoleon operation

Fig. 5A

Fig. 5B

Fig. 6A

Fig. 6B

Pre- and Postoperative Clinical Photographs

FIG. 7A

FIG. 7B

FIG. 8A

FIG. 8B

FIG. 9A

FIG. 9B

PRE- AND POSTOPERATIVE CLINICAL PHOTOGRAPHS

further. Some have performed total excision of the elephantoid tissue from the limb followed by skin grafts, the skin over the excised elephantoid tissue being used for grafting. But they have made no mention of having excised the deep fascia. This is important, for, in all these cases, the deep fascia is sclerosed, hard as cartilage and often calcified due to recurrent attacks of inflammation. The few normally existing apertures in the deep fascia are found completely occluded and an impenetrable barrier between the superficial and deep lymphatics was present in elephantoid states.

The third series of cases in the group operated on had the benefit of the modified Kondoleon operation. This operative technique has afforded prolonged if not permanent relief to many of the patients. This is substantiated by the pre- and postoperative clinical photographs (Figs. 5-9).

Preoperative care of the patient and the details of operation are recorded below:

1. Care is exercised to eliminate focal and local sepsis by appropriate measures. Nutritious food, liver extract, iron and vitamin B complex were given to overcome undernutrition and anaemia. The skin is prepared for operation by the usual method. The patient is given a prophylactic dose of A.T.S.

2. 6-9 c.c. of 1 in 1500 light nupercaine intrathecally was the anaesthetic of choice. This brought down the blood pressure to the desired level to minimise bleeding from the extensive area to be excised. Soon after the administration of the anaesthetic the limb is held up for about 5 minutes.

3. A tourniquet is then applied over the midthigh region.

4. Large Thiersch skin grafts are then prepared from the elephantoid tissue by means of an ordinary cut throat razor. As the skin is stretched over the elephantoid tissue, preparation of skin grafts is extremely easy. They are preserved in warm saline.

5. A transverse incision is made across the posterior aspect of the leg at the proximal end of the gross lesion and the veins are ligatured at both ends to prevent bleeding, while dissecting the elephantoid tissue below. The patient is now turned on to his back or the limb is flexed while the dissection on the anterior aspect is in progress.

6. The transverse incision mentioned above is extended anteriorly over the proximal end of the growth. Bleeding is controlled by doubly ligaturing the severed veins.

7. The elephantoid tissue is excised *in toto* below the transverse incision. This is done conveniently through a vertical incision extending from above downwards on to the foot, and in depth to the deep fascia. The flaps are dissected outwards exposing the deep fascia covering the entire limb. The dissection on the posterior aspect of the limb is facilitated by supporting the limb over a wooden block covered with sterile towels.

8. 40 minutes is the maximum time taken for the excision of elephantoid tissue, then the tourniquet is released. Meanwhile all the bleeding points are ligatured and further bleeding, if any, is controlled by hot packs.

9. Two vertical windows each 4" × 4" are made by excising the deep fascia, one on the inner and the other on the posterior aspects of the limb and a third small one is created on the dorsum of the foot.

10. The entire raw surface is then dusted with sulphanilamide powder. Penicillin solution 0·1 million units in 10 c.c. is instilled over the raw area by means of a syringe. Thiersch's skin grafts are now applied

to cover the raw area, fixing them by sutures at random points.

11. The area is covered with large sheets of vaseline gauze after dusting with sulphanilamide powder a second time. Occlusion plaster is now applied tightly without any cotton pads intervening. The occlusion plaster is removed 10 to 12 days after the operation. The results of skin grafting are extremely gratifying. In the later cases the incision is made deep to the muscles, and the elephantoid tissue along with the deep fascia is shelled out from all over the limb exposing the muscles. The skin grafts are then applied. This procedure has the double advantage of less bleeding and duration of operation is greatly reduced.

In case the scrotum is also the site of elephantiasis, the cord along with the testis is implanted on the corresponding side in the intramuscular plane after cutting through the deep fascia of the thigh, instead of reposing it in subcutaneous pouches. The rationale of this is similar to the implantation of the spermatic cord with its chain of lymphatics in the inguinal region by Lantz in 1911 with the object of constructing a lymphatic bridge across the blocked inguinal region between the abdominal and the deep lymphatics of the thigh through the spermatic cord.

The patients are required to stay for about 60 days in hospital of which 30 days are taken up for preoperative treatment. The chances of postoperative shock supervening in these cases are remote and are minimised by the immediate covering of the raw surface with skin grafts supplemented by pressure bandage or occlusion casing by P.O.P. A point or two of plasma or blood is always kept in reserve to combat any threatened shock. There has been no mortality in the 50 cases of elephantiasis of legs so treated surgically. During the follow up of three cases, fissures and cracks on the dorsum of the foot discharging serous fluid were noticed. Much improvement in their condition was observed by oral iron, parenteral administration of vitamin B-complex and cod liver oil dressings. Evenness in the operated limb was induced by elastic bandages over the skin-grafted surface for a month. Cases are being followed up.

SUMMARY

1. Histological study of the excised elephantoid tissue revealed perivascular infiltrate of round and plasma cells with abundant increase in fibrous tissue and lymphangitis and endophlebitis and occasional dead microfilaria.

2. Details of the modification of the original Kondoleon operation for surgical treatment of elephantoid legs as practised by the author are recorded. The necessity to excise elephantoid tissue down to the deep fascia and sacrificing the latter in places to establish free circulation between the superficial and deep lymphatics is emphasised.

3. The Kondoleon operation as modified by the author is not time consuming and is free from postoperative complications. Healing occurred in a surprisingly short time. The patients were afebrile throughout the postoperative period.

ACKNOWLEDGMENT

I am grateful to Dr. D. Jaganatha Reddy, for both the biopsy report on the excised elephantoid tissues and photomicrographs and also to Dr. K. V. Subbarao. My thanks are also due to Dr. A. N. Ramanathan, and Dr. B. Ramanarayana Murthy, for the biochemical and bacteriological reports respectively.

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LIVER FUNCTION TESTS IN NUTRITIONAL ANAEMIAS

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AND

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Composite liver function tests have been carried out in persons suffering from diverse liver diseases by workers all over the world. Though liver dysfunction due to damage of parenchyma cells of the liver has been supposed to be brought about, amongst other things, by anoxia due to low oxygen carrying capacity of the anaemic blood, composite liver function tests have not been extensively carried out in cases of anaemias.

That there is some relation between the liver and anaemia is evident from the following observations:

(1) *Clinically*—hepatomegaly is seen in a number of cases.

(2) *Pathologically*—fatty changes in the liver have been reported in cases of moderate to severe degree of anaemia.

(3) *Therapeutically*—satisfactory response with liver preparations has been noted in different types of anaemia.

To elucidate these points composite liver function tests were carried out by Schilling and Harris (1952) in 20 cases of pernicious anaemia and 6 cases of nutritional megaloblastic anaemia. They did not find any regular pattern of hepatic dysfunction either in pernicious anaemia or in nutritional megaloblastic anaemia.

The present study was undertaken to find out whether anaemia *per se* causes liver dysfunction and whether the rate of clinical and haematological improvement is in any way influenced by liver dysfunction.

Materials and Methods

To determine the various functions of the liver viz., protein metabolic function, detoxifying function and excretory function different tests were carried out to evaluate the different functions in anaemia and to find out the correlation, if any, of the different liver functions with the type and degree of anaemia.

I. *To determine the protein metabolic function* the following tests were carried out:

(a) Thymol turbidity test.

(b) Plasma prothrombin activity and its response to vitamin K.

(c) Total plasma protein and albumin and globulin ratio.

II. *To determine the detoxifying function* the following tests were carried out:

(a) Hippuric acid test.

(b) Brom-Sulfalein test.

III. *To determine the excretory function* the following test was carried out:

Van den Bergh reaction

Summary of the Methods Employed:

I (a) *Thymol turbidity test* (Maclagan, 1944)—9 c.c. of thymol buffer pH 7·8 (sodium barbital 1·03 g., barbital—1·38 g., thymol—3 g., distilled water 500 c.c.) was added to 0·15 c.c. of the serum and was kept for half-an-hour till the solution turned turbid. Turbidity was measured in photo-electric colorimeter and expressed in units by comparison with a standard curve prepared by uses of barium sulphate suspension (Shank and Hoagland, 1946).

Normal limit is 0-4 Maclagan unit. Higher values would indicate derangement of protein metabolic function.

(b) *Plasma prothrombin activity and its response to vitamin K* (Kark and Souter, 1941)—For prothrombin estimation, modified Quick's method was adopted using acetone dehydrated human brain substance as the source of thromboplastin. After a basic estimation of prothrombin, 10 mg. of vitamin K was injected intramuscularly. Twenty four hours later, plasma prothrombin activity was re-estimated and any increase of prothrombin was expressed as percentage increase over the basic level.

In normal controls the prothrombin activity after vitamin K, increased by 10 to 20 per cent. Lower prothrombin response signifying defective prothrombin synthesis by the liver is indicative of deranged protein metabolism.

(c) *Total plasma protein and albumin: globulin ratio*—Micro Kjeldahl method was adopted for the determination of protein.

Low total protein and/or altered albumin/globulin ratio are suggestive of disturbed protein metabolic function.

II (*a*) *Hippuric acid test* (Quick, 1938)—The test was done in the morning after breakfast.

(1) The patient emptied his bladder and drank a glass of water.

(2) Sodium benzoate solution (1·77 g. in 20 c.c. of distilled water) was injected intravenously very slowly over a period of from 5 to 10 minutes (rapid injection may cause nausea and vomiting).

(3) For one hour the patient was kept in the bed and was not allowed to take any food or to pass any urine.

(4) At the end of one hour the patient again emptied his bladder as completely as possible and the urine was collected for examination.

(5) The urine was measured and 5 g. of solid ammonium sulfate was added for every 10 c.c. of urine. The urine was then filtered.

(6) The solution was acidified with conc. HCl and was shaken vigorously until precipitation of hippuric acid was complete. It was kept in refrigerator for one hour.

(7) It was then filtered and the crystals of hippuric acid washed with iced water.

(8) The crystals were dissolved in 500 c.c. of hot water and the solution titrated against 0·2 N NaOH using phenolphthalein as the indicator. Any free HCl, if present, was titrated first with Topffer's reagent prior to estimation of hippuric acid.

Calculation: One c.c. of 0·2 N NaOH is equivalent to 0·0358 g. of hippuric acid; therefore the amount of NaOH in c.c. multiplied by 0·0358 would give the amount of hippuric acid in gramme. To this figure this obtained add 0·1 g. for every 100 c.c. of urine representing the amount of hippuric acid originally left in solution to get the actual amount of hippuric acid excreted along with the urine in one hour.

Normal excretion of hippuric acid should be approximately 0·7 g. or more for the first hour. Excretion less than 0·7 g. is definitely indicative of depressed liver function.

(b) *Bromsulfalein test*—Macdonald's (1939) modification of Rosenthal and White's method (1925).

5 g. of the dye per kilogram of body weight (in the form of 5 per cent solution) was injected slowly by the intravenous route. Two samples of blood 4-5 c.c. each were collected exactly 15 and 45 minutes after the injection. The samples were allowed to clot and then centrifuged to get the clear serum. The serum was poured into two small test tubes; to one of these was added one or two drops of 10 per cent solution of NaOH to bring out the colour of the dye and to the other tube a drop of 5 per cent HCl to clear the serum of any haemolysis. The amount of dye present was estimated by direct comparison with a series of standards. The tube of clear acidified serum was placed in front of the standard in a comparator block for

TABLE I

		Thymol turbidity test		*Prothrombin response to vit. K*		*Total protein*		*Albumin-globulin ratio*		*Hippuric acid test*		*Indirect van den Bergh test*	
		NORMAL	HIGH	NORMAL	LOW	NORMAL	LOW	NORMAL	LOW	NORMAL	LOW	NORMAL	HIGH
Macrocytic (21)	Before treatment	10	11	15	4	12	8	12	8	9	11	18	3
	No. examined after improvement of blood picture	8	5	11	3	7	6	8	6	6	10	14	3
	No. in which results changed*	2	3	4	0	0	5	6	2	0	8	0	3
Dimorphic (27)	Before treatment	21	6	14	12	22	5	12	15	14	13	22	5
	No. examined after improvement of blood picture	13	3	9	8	9	2	7	4	6	10	19	3
	No. in which results changed*	5	1	1	6	2	2	1	4	0	10	0	3
Hypochromic (9)	Before treatment	7	1	5	3	7	1	2	6	4	4	8	0
	No. examined after improvement of blood picture	4	1	4	3	1	2	1	2	4	4	5	0
	No. in which results changed*	1	1	2	3	0	2	0	2	0	4	0	0
All types of anaemia (56)	Before treatment	38	18	34	19	41	14	26	29	27	28	48	8
	No. examined after improvement of blood picture	25	9	24	14	17	10	16	12	16	24	38	6
	No. in which results changed*	8	5	7	9	2	9	7	8	0	22	0	6

N.B.—Figures under 'Normal' column indicate the no. of cases in which the hepatic function deteriorated i.e. became abnormal from a basic normal level. Figures under columns 'High' or 'Low' indicate the no. of cases in which initial abnormal hepatic function became normal after treatment.

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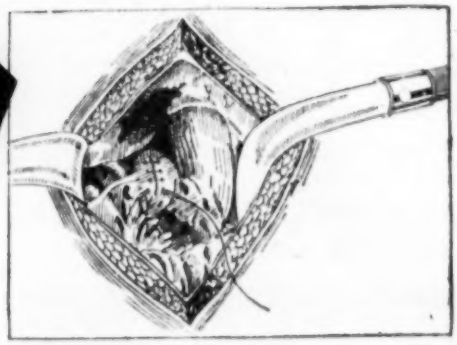

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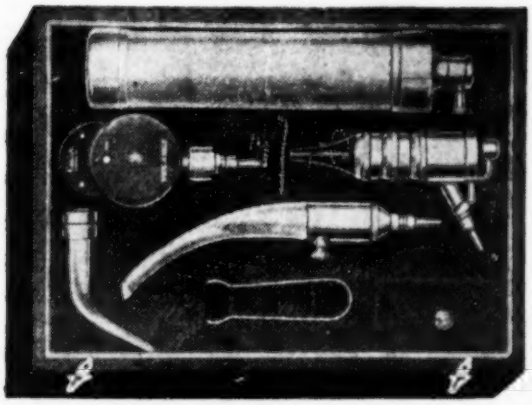

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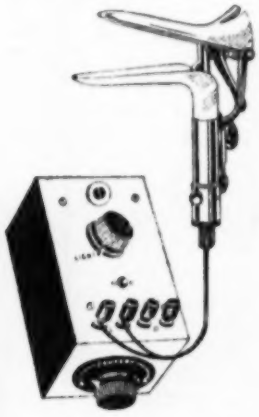

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comparison with a coloured alkalinised serum by simultaneously looking through both tubes.

The standard was prepared by adding 4 g. of bromsulfalein to 100 c.c. of water alkalinised with 0·25 c.c. of 10 per cent solution of NaOH. This represented 100 per cent standard. By proper dilutions with similarly alkalinised water 10 standards were prepared ranging from 10 to 100 per cent. 5 c.c. of each standard solution was sealed in a small test tube and kept in the dark.

Normal range according to Mateer *et al* (1942) is that 15 minutes' sample should not contain more than 25 per cent and 45 minutes' sample not more than 4 per cent of the dye.

III. *Van den Bergh Test*—It was done according to the method of Thannhauser and Anderson (1921) using a Lovibond comparator. Total bilirubin content of plasma was estimated in mg. per 100 c.c. of blood. Normal value in Indians is 0-1 mg. per 100 c.c. of the blood. Higher values indicate deranged excretory function of the liver.

Fifty-six indoor patients admitted to the Carmichael Hospital for Tropical Diseases were studied in the present series (Table 1).

The different liver function tests were performed soon after admission and before administration of any specific drug. Tests were repeated whenever any particular test showed values widely divergent from others. All the tests, in identical way, were repeated in 34 patients before their discharge from the hospital and at a time when there had been considerable clinical and haematological improvement.

The nature and degree of anaemia in the different patients are shown in Table 2.

TABLE 2

Types of anaemia	*R.B.C. 0-1·5 m.*	*R.B.C. 1·5-3·0 m.*	*R.B.C. 3·0 and above*	*Total*
Macrocytic ...	10	10	1	21
Hypochromic ...	2	6	1	9
Dimorphic ...	13	14	—	27

ANALYSIS OF DATA

I. PROTEIN METABOLIC FUNCTION:

(a) *Thymol turbidity test*—High values over 4 Maclagan units were found in 50 per cent cases of macrocytic anaemia, in 22 per cent cases of dimorphic anaemia and in 12 per cent cases of hypochromic anaemia. In the different types of anaemia, there was no correlation between the rate of improvement and derangement of liver function as shown by this test. Repetition of the test after clinical and haematological improvement did not show any correlation between the clinical and haematological states of the patients and this liver function test. After low initial value, higher values were sometimes found after clinical and haematological improvement.

Irrespective of the type of anaemia high initial values were found in 50 per cent of the cases having enlarged spleen and liver, in 27 per cent of the cases with enlarged liver only and in 33 per cent of the cases without any enlargement of spleen and liver. Thus enlargement of liver alone did not give high values but enlargement of the spleen and liver did.

(b) *Prothrombin response to vitamin K*—Basic prothrombin level was below 80 per cent in 44 per cent of the total cases and tthe incidence of hypoprothrombinaemia was highest in the macrocytic group. Inadequate response to vitamin K injection was found in 36 per cent in the series, the response being poorest in the macrocytic group. Inadequate response was most frequent in the cases with enlarged liver, particularly in the dimorphic group. There was no correlation between basic prothrombin level and response to vitamin K. Repetition of the test after improvement did not always show increased basic level or improved response.

(c) *Total protein and albumin: globulin ratio*—Low plasma protein was found in 40 per cent cases of macrocytic anaemia, in 18 per cent cases of dimorphic anaemia and 12 per cent cases of hypochromic anaemia, while altered albumin: globulin ratio due to altered albumin-globulin ratio was found in 75 per cent cases of hypochromic anaemia, 55 per cent cases of dimorphic anaemia and 40 per cent cases of macrocytic anaemia. Thus altered albumin globulin ratio was seen in larger number of patients but in the different types of anaemia, there was no correlation between low plasma protein and altered albumin globulin ratio in the same person. No correlation was also seen between the improvement rate and the total protein or albumin globulin ratio in the different types of anaemia.

Repeat examinations after improvement of blood picture showed increase in total protein in a number of cases with initial low plasma protein, but generally no improvement of the albumin: globulin ratio was noted; on the contrary albumin globulin ratio was found to have been lowered in a number of cases.

Total protein level or albumin: globulin ratio had no correlation with enlargement of liver and/or spleen. On the contrary altered albumin: globulin ratio was found in a larger number of cases without any enlargement of spleen or liver.

Response to the above tests varied with the type of anaemia, for example, higher values for the thymol turbidity test were found mostly in the macrocytic group, prothrombin response to vitamin K was poorest

in the dimorphic group while altered albumin: globulin ratio showed maximum incidence in the hypochromic group.

Repeated examinations after haematological improvement did not show any strict correlation between the improvement of the patient and the different liver function tests except however, in case of total plasma protein which constantly increased with the clinical and haematological improvement of the patient. With improvement, albumin: globulin ratio was found to have changed towards normalcy in the dimorphic and hypochromic groups but not usually in the macrocytic group. Thymol turbidity test gave variable results and not infrequently cases with low initial value showed higher values after considerable clinical and haematological improvement. This was particularly observed in the macrocytic group. Enlargement of the liver appeared to have some adverse influence on the response to vitamin K but not on the other two tests.

From the data available indication regarding the improvement of the patients may be obtained from plasma protein studies in all types of anaemia particularly in the cases showing low initial plasma protein level. But on the whole none of the above tests are of much help as a guide to the diagnosis and prognosis of any particular type of anaemia.

II. Detoxifying Function:

(a) *Hippuric acid excretion test*—Initial values for hippuric acid excretion was low in 55 per cent cases of macrocytic, 48 per cent cases of dimorphic and in 50 per cent cases of hypochromic anaemia. In the cases with low initial excretion, the excretion was found to have increased considerably in almost all the cases after satisfactory clinical and haematological improvement. This increase was seen in all the cases irrespective of the type of anaemia and the rate of improvement. A definite correlation was noted between diminished excretion and the degree of anaemia —this correlation was more marked in the dimorphic anaemia. Diminished excretion was noted in 50 per cent of the total cases. Of the cases showing poor excretion, 24 per cent had hepatosplenomegaly, 24 per cent had hepatomegaly and 52 per cent showed no palpable enlargement of liver and spleen. Thus there was no significant correlation between the excretion pattern and the enlargement of liver and/or spleen.

The present study would indicate that the detoxifying function of liver is diminished in all anaemias and that the function is restored with the improvement of anaemia, but this has no correlation with the enlargement of spleen and liver.

(b) *Bromsulfalein excretion* test was carried out only in 10 patients of which 5 were macrocytic, 3 dimorphic and 2 hypochromic in type.

Retention of the dye after 15 minutes was high in all the cases excepting one in the macrocytic group.

Retention after 45 minutes was high in all three cases of dimorphic anaemia, 2 cases of macrocytic anaemia and 1 case of hypochromic anaemia.

High retention values had no definite correlation either with the degree of anaemia or with the hepatosplenomegaly.

After clinical and haematological improvement repetition of the test in 2 cases of macrocytic anaemia did not show any improvement of this particular function of liver. Repetition of the test in 2 cases of dimorphic anaemia, however, showed improved function in 1 case.

III. Van den Bergh Reaction:

Plasma bilirubin level was over 1 mg. per cent in 14 per cent cases of macrocytic type and in about 18 per cent cases of dimorphic type. With improvement the values came back to normal level in all the cases.

There was however no definite correlation of hyperbilirubinaemia with either the degree of anaemia or with the rate of improvement. Higher values were usually found in the cases with moderate to high degree of splenomegaly.

Discussion

Abnormalities of liver functions as measured by the different tests were found in a number of cases. No consistently abnormal pattern was, however, seen in the different types of anaemia, or in the same patient before and after haematological improvement, and thus our results are in general agreement with the results of Schilling and Harris (1952) in cases of pernicious anaemia and nutritional megaloblastic anaemia. We do not however, agree with these workers that anoxic stress would not produce any abnormality of liver function demonstrable by assay methods. In the present study, detoxifying function of the liver as measured by hippuric acid excretion test was found to be considerably diminished in all types of anaemia. The diminished excretion had definite correlation with the degree of anaemia. This diminished function was uniformly restored with the improvement of anaemia. Evidence of derangement of protein metabolic function of the liver was afforded by low total protein values found in a large number of cases of macrocytic anaemia, and this function also, was usually restored with the improvement of blood picture. Normalisation of liver dysfunctions with the improvement of blood picture would indicate that in some cases at least anaemia anoxia is responsible for liver dysfunction. But in the absence of any constant correlation between the degree of anaemia and the various liver function tests, it is presumed that in addition to anaemic anoxia there are other factors which exert deleterious effect on the liver parenchyma cells and produce abnormalities of liver function.

ACKNOWLEDGMENT

This study was carried out with the award of a Fellowship by the Teddington Chemical Factory (Bombay) and our grateful thanks are due to them. We are very thankful to Dr. J. B. Chatterjea for his helpful and valuable suggestions.

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AN ENVIRONMENTAL FACTOR INFLUENCING THE TOXICITY OF INTRAVENOUS IRON

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The rapid improvement in the haemoglobin level of iron-deficiency anaemias by intravenous iron is now well known in therapeutic practice. Though simple in preparation the product, however, has a tendency to cause untoward reactions, and the cause of its delayed introduction in therapeutics is mainly due to this factor. Nissim and Robson (1949) have reported the LD50 of an intravenous iron preparation to be 300 mg/kg. Inspite of toxicity passing at such dose level, —reports of reaction in human cases have been reported by Barrit and Swain (1953).

In this Laboratory a large number of batches of intravenous iron preparation by an Indian firm has been subjected to acute intravenous toxicity tests in comparison with some well known similar products of other countries. Significant variation in the toxicological data was observed during these studies.

The tests were carried on inbred white mice of fixed average weight of 15 g., severe care being taken that the individual weights did not vary more than 0·25 g. The animals were fasted for 3 hours before injections. The drug was used in a dilution of 1 in 2. The diluent used was both physiological saline and redistilled water. The test chosen was 100 mg. per kg. and was worked out by administration of several doses of a standard foreign preparation.

CONCLUSION

It was observed consistently that the lethal dose of any particular sample varied with the season. A dose which was low in toxic manifestation during winter, gave high mortality figures in the hot summer months. In autumn the degree of tolerance was more than that during the summer months.

It was further observed that the contents of ampoules once broken, could not be used even after careful re-sealing. Such a procedure always increased the toxicity of such a preparation. It is, therefore, likely that ampouling may exert an influence on the development of toxicity in the material. On account of these important factors modifying the toxicity of intravenous iron, it has been seldom possible to confirm the data on toxicity as reported by workers and as claimed by the manufacturers. It appears probable that the

TABLE 1—SEASONAL VARIATION IN THE TOXICITY OF INTRAVENOUS IRON PREPARATIONS

Preparation	*Date of testing*	*Dose mg/kg.*	*No. of mice*	*Mortality*	*% Mortality*	*Remarks*
No. 164	1-12-52	100	5	0/5	0	Winter
,,	5-1-53	,,	5	1/5	20	,,
,,	19-2-53	,,	10	4/10	40	Winter passing
,,	11-3-53	,,	10	7/10	70	Summer started
No. 185	20-3-53	100	10	3/10	30	Summer started
,,	23-4-53	,,	10	6/10	60	Very hot
,,	10-7-53	,,	10	1/10	10	Cool (due to rains)
No. X	21-1-52	300	2	0/2	0	Winter
	21-1-52	400	2	0/2	0	,,
	28-2-52	400	4	3/4	75	Winter passing
Indian Product	20-3-53	100	10	1/10	10	Summer started
	15-4-53	,,	10	5/10	50	Very hot
	7-5-53	,,	10	2/10	20	Cooler with Norwester
	14-5-53	,,	10	7/10	70	Very hot
	19-5-53	,,	10	6/10	60	,,
	25-6-53	,,	10	6/10	60	,,
	10-7-53	,,	10	5/10	50	Cool (due to rains)

dosages as reported (Barrit and Swain, 1953) for LD50 were carried on mice kept at a much lower temperature than that available in the tropics. As such, the increased environmental temperature of the tropical countries has caused an increase in the toxicity of the same preparation, when tested under tropical conditions.

One very important inference from such a finding is the possibility of having some unusual reactions in iron preparations in the tropics when tested in hot summer months, and it would be advisable for the physician using the product to keep such changes in mind when pursuing intravenous iron therapy.

Summary

1. The toxicity of some market preparations of intravenous iron and samples prepared by an Indian company has been studied at different periods of the year. The test dose on the basis of LD50 was determined to be 100 mg/kg.

2. It has been observed that the LD50 dose varies with the seasons. In hot summer, the dose is significantly high, while in cold winter months it is more tolerable.

3. The probability of meeting with untoward reactions following intravenous administration of iron to human patients, during the summer months is also stressed.

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STUDIES ON THE PHYSIOLOGY OF NASAL PASSAGES

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It has been observed by several patients with nasal catarrh and obstruction of one nostril, that lying on the side with the face turned so that the affected nostril was above, often brought about relief and increased air flow through that passage. The following experiments were undertaken with a view to investigate this interesting observation in relation to the effect of posture on the relative patency and airflow in the two nasal passages.

Leib and Mulinos (1939) studied the effect of posture on nasal patency using the modified Glatzel's mirror. They found no alteration in relative patency of the nasal passages on changing from the sitting to the supine position. But, lying on the side, they found, partial to complete obstruction of dependent side was usually produced, and when the relative position of nostrils were reversed, the previously dependent side began to open and the newly dependent side to close.

Using the technique described in a previous paper (Singh *et al*, 1954) simultaneous records for both nasal passages were obtained with the subjects under study in five different postures in the order given below:

1. Standing.
2. Sitting comfortably in an arm chair.
3. Lying in the supine position.
4. Lying on the right side with the face turned so that the right nostril was in the dependent position.
5. Lying on the left side with the left nostril in the dependent position.

After recordng the graph in one position, the posture was changed to the next, and an interval of 10-15 min. was allowed to lapse before the next recording, so that breathing might reach the restful level in that posture. The first series of experiments were conducted on apparently normal individuals. Records of four subjects are presented (Fig. 1).

On changing from the standing to the sitting, or from sitting to the supine position there was no alteration in the relative patency of the two nasal passages. Lying on the right side with the right nostril in the dependent position, the amplitude of graph for the right nasal passage decreased and that of the left increased. Lying on the left side, with the relative positions of the nasal passages reversed, the results were also correspondingly altered. In both these positions, it was seen that the dependent nasal passage became less patent, while the other became more patent.

Three patients with deflected nasal septum and symptoms of obstruction were studied. The graphs of two of these patients are presented and show the same results (Fig. 2).

Though the number of cases studied by the use of this technique is small, our findings confirm the results obtained by Lieb and Mulinos, using rhinohygroscopic methods.

In the light of these findings, it is worth while considering the following points:

(*a*) Though a subject with approximately equal lumens on both sides may not feel any difference in comfort, a person with unequal lumens will feel less comfort when he is lying with the narrower nostril in the dependent position and would prefer to lie with that passage on the upper side. It may be very useful instruction or rule for the persons with unequal lumens to lie on the side which has the wider lumen. Though the latter may be narrowed, a little, it will not produce discomfort while the narrower one taking up a higher position will be wider and cease to be a source of discomfort.

(*b*) Even in normal persons with nearly equal lumens when subjected to common cold, and unequal

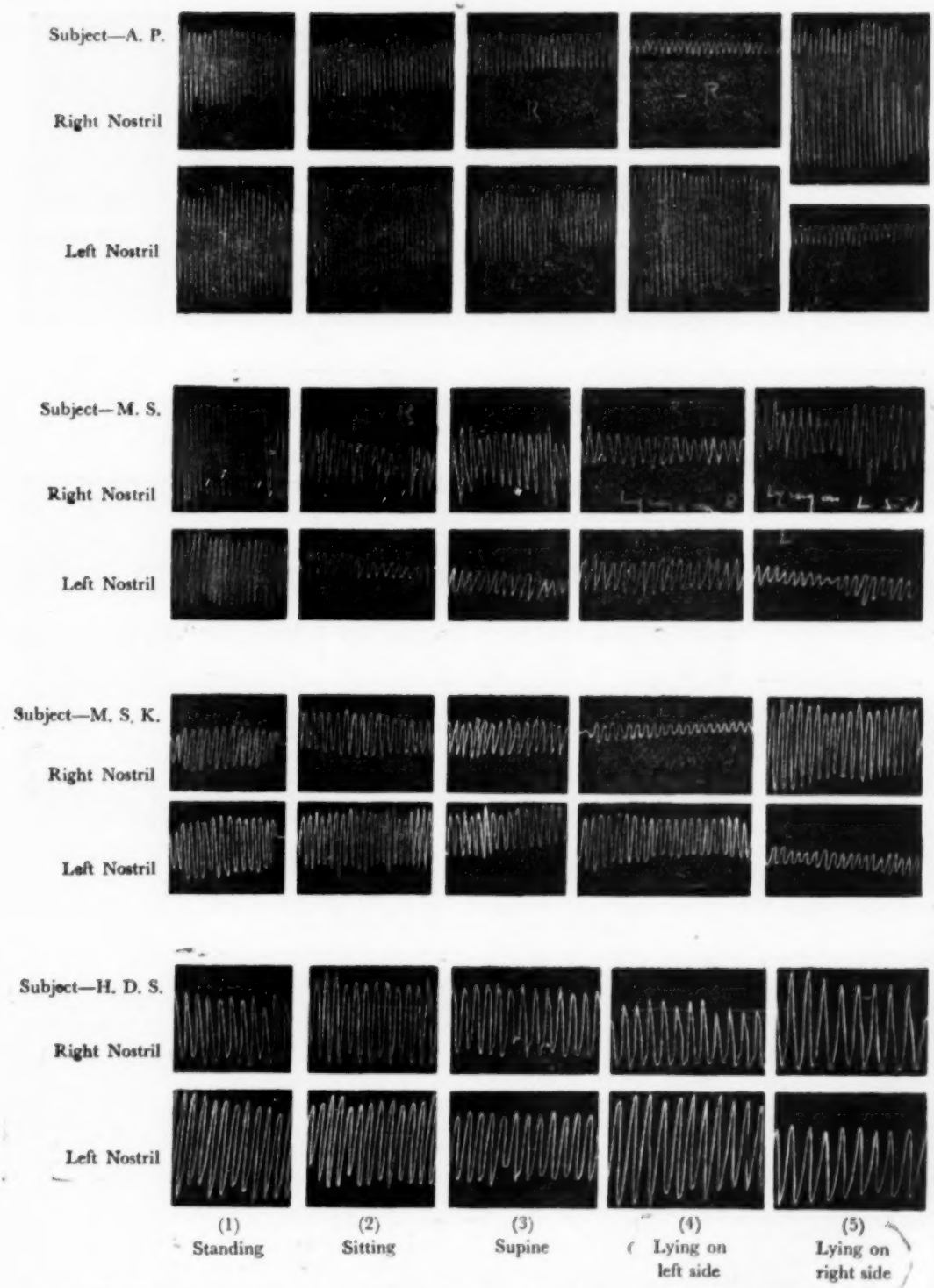

FIG. 1—GRAPHIC RECORDS OF NASAL AIR FLOW ON THE TWO SIDES SHOWING VARIATIONS WITH CHANGES IN POSTURE (4 NORMAL SUBJECTS)

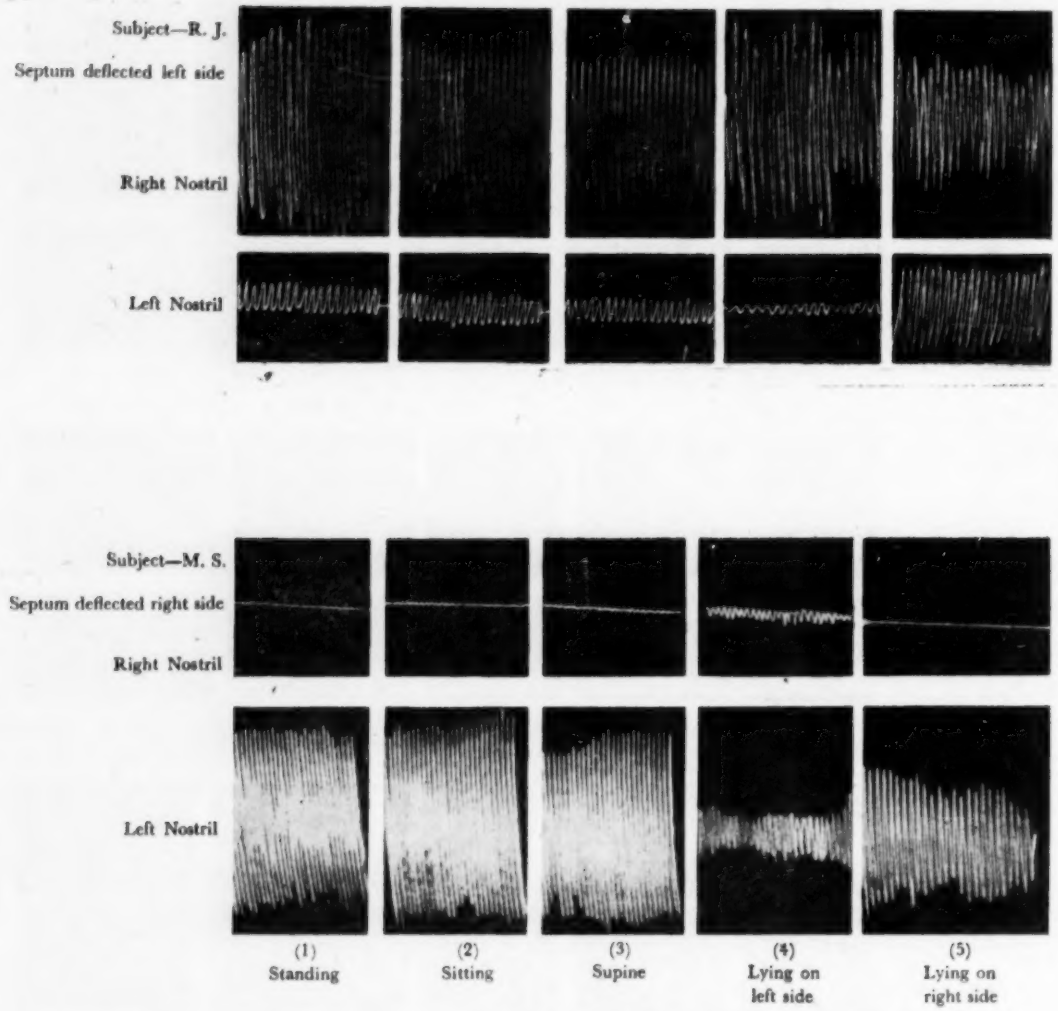

FIG. 2—GRAPHIC RECORDS OF NASAL AIR FLOW ON THE TWO SIDES SHOWING VARIATIONS WITH CHANGES IN POSTURE (2 SUBJECTS WITH DEFLECTED SEPTUM)

nasal congestion, the change of position may afford some relief.

(*c*) It is worthwhile observing the position taken up by some persons, during sleep to study whether the relative patency of the nasal passages has anything to do with a preference for a particular position.

SUMMARY

Study of simultaneous records of air flow through the two nasal passages, obtained by connecting the nostrils with rubber tubes to two Brodies' tambours, indicates that there is no alteration in the relative patencies of the two nasal passages on changing from the standing to the sitting, or sitting to the supine position. But, when lying on the side the dependant nasal passage becomes narrower, while the upper of the two passages has a larger calibre.

It is suggested that this observation may be utilised in relieving the discomfort caused by permanent or transient variations in the relative patency of the nasal passages due to deflected septa, or catarrhal and other conditions.*

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*Read before the Physiology Section of the Indian Science Congress, Hyderabad (Deccan) January 1954.

SPECIAL ARTICLE

PROGRESS IN ANTIBIOTIC THERAPY

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There has been considerable progress in antibiotic therapy in recent years. Newer antibiotics are being continuously introduced in medical practice and the uses of the older ones are being subject to many changes. The development of drug resistance has also raised a serious problem. All these call for renewed evaluation of the status of the existing antibiotics in therapy. In the present review an attempt has been made to indicate the chief lines of progress and assessment in recent years. However, it can hardly be a comprehensive one and only some of the newer developments and their implications in clinical practice are dealt with.

New Antibiotics: Erythromycin (Ilotycin) and Magnamycin (Carbomycin)

These two new additions to the existing list of antibiotics have an antibacterial spectrum resembling more or less that of penicillin. They are effective against the Gram positive bacteria: staphylococci, streptococci, pneumococci, C. diphtheriae and against Neisseria and Haemophilus group. A comparative clinical evaluation of these drugs has yet to be made. The minimum inhibitory concentration of erythromycin is lower than that of magnamycin (Welch *et al*, 1952) and both appear to be somewhat less potent than penicillin against most infections (Finland, 1953).

It is an advantage that these antibiotics are active against organisms that are resistant to penicillin or other antibiotics. The importance of the problem will be realised from a report from a hospital in the U.S.A. (Finland and Haight, 1953) where 70 per cent of staphylococcal infections were found to be resistant to penicillin and 40-60 per cent to aureomycin and terramycin. Penicillin resistant organisms have also been isolated from the throat of 20 per cent of the hospital staff (Needham and Nichols, 1953. The new antibiotics are, therefore, a welcome addition to the drugs that may be used for organisms resistant to one or more antibiotics. Erythromycin will be particularly useful in staphylococcal infections where penicillin owing to the high incidence of drug resistance, is no longer considered the drug of choice. *In vitro* sensitivity testing with different strains of staphylococci shows that this organism is proving resistant to all antibiotics in use. None of the strains are however so far naturally resistant to erythromycin (Finland and Haight 1953; Haight and Finland, 1952a). The drug has been "life saving" in a type of staphylococcal enteritis otherwise not amenable to treatment with penicillin, streptomycin or some of the other broad spectrum antibiotics (M. R. C. Report, 1954; Dearing and Heilman, 1953). Unfortunately resistance to erythromycin and magnamycin may also develop rather rapidly and there is considerable cross-resistance between the two (Fusillo *et al*, 1953; Hobson, 1954). This restricts the value of having two drugs and virtually makes one only available for therapy of infections produced by organisms resistant to other antibiotics. Erythromycin and magnamycin have been found to be effective against Str. faecalis and Str. viridans but their use in bacterial endocarditis caused by these infections is often limited by the development of drug resistance (Haight and Finland, 1952b). Erythromycin may, therefore, be used more successfully in such cases in combination with antibiotics like penicillin, streptomycin or bacitracin which improve activity and delay the development of resistance (Finland, 1953; Purcell *et al*, 1953).

The antimicrobial range of both erythromycin and magnamycin are believed to extend also to brucella, rickettsia, some larger viruses and *E. histolytica* (Oscar Urteaga *et al*, 1953; Tanner *et al*, 1952; McGuire *et al*, 1952). Erythromycin, which has had more clinical trials, is usually administered in a dose of 300-500 mg. 6-8 hrly.; even a lower dosage may be used in milder infection. It is relatively non-toxic but mild gastro-intestinal disturbance may occur with higher doses. One of the advantages claimed for erythromycin is its lesser interference with intestinal flora, coliform organisms are unaffected and moniliasis does not develop (Tice, 1953). Both erythromycin and magnamycin appear in the bile but while the former is excreted by the kidney, very little of the latter drug is present in the urine. Erythromycin traverses the placental barrier and appears in serous effusions but does not readily diffuse to the cerebrospinal fluid (Heilman *et al*, 1952) where only low concentrations may be attained (Haight and Finland, 1952c; Smith *et al*, 1953). This explains its failure in a case of pneumococcal meningitis which subsequently responded to penicillin (Grigsby, 1953).

The antibiotics will have to be clinically assessed carefully before their place in treatment can be properly ascertained. As it stands now, they undoubtedly provide an alternative for penicillin in case of resistant organisms or sensitive persons. In such cases one may prefer to use erythromycin (within its antibacterial range) rather than a broad spectrum antibiotic like the tetracyclines or chloramphenicol because of the lesser disturbance with the bacterial flora. Comparative studies with the broad spectrum antibiotics show that it is more active against Gram positive organism and less against Gram negative bacilli except haemophilus where it is equally active (Haight and Finland, 1952a).

The readiness with which organisms may become resistant to erythromycin (resistant organisms have been recovered even from nose and throat of the staff of hospital where the drug has been in general use), however, calls for caution (Lepper, 1953) and the risk of building up a staphylococcal population resistant to

erythromycin in addition to earlier antibiotics has to be remembered. It is enjoined, therefore, that the drug should be prescribed with due regard to the danger of indiscriminate use and 'penicillin should be preferred, on this ground—and, it may be added, that of economy—when it will serve equally well' (M. R. C. Report, 1954). Erythromycin, to be of maximum service should be used with a more specific aim and objective as outlined above.

PENICILLIN, TETRACYCLINES, CHLORAMPHENICOL, ETC.

Penicillin has had an unique position in its freedom from toxicity even in massive doses. However, more frequent reports are now coming of untoward reactions of an allergic nature with an incidence of 2·5 per cent in one group of 10,000 cases (Thomas *et al*, 1948). Contact dermatitis may follow topical application (Council of Pharmacy and Chemistry, 1950). The reactions after systemic administration may occasionally lead to serious exfoliative dermatitis or anaphylaxis ending fatally (Walabat, 1949; Ravinovitch and Snitkoff, 1948; Flaxan, 1951; Siegal *et al*, 1953; Feinberg *et al*, 1953). Severe Jarish Herxheiner reaction in syphilis (Flaxan, 1951), haemorrhagic necrotic lesions (Rubens, 1951), periarteritis nodosa (Surdakowski, 1954) and Loeffler's syndrome (Reichlin *et al*, 1953) have also been reported. The antibiotics may attain high concentration in presence of renal dysfunction and intravenous administration of 12 million units of penicillin every 4 hours or 4-28 g. of terramycin in 4 to 17 days in patients with neoplastic diseases caused many fatalities (Bateman *et al*, 1952). Hypersensitivity reactions have been known to occur against other antibiotics though possibly less frequently than with penicillin and streptomycin (Barach *et al*, 1952). The incidence of severe reaction with penicillin, however, is still very low and it remains the safest antibiotic if precautions are taken to avoid allergic reactions. For that matter, its indiscriminate use and topical applications may be abandoned. History of past reactions or other allergic symptoms should make one cautious. Either a different antibiotic may be used or it may be given after testing and with increasing desensitising doses under cover of an antihistaminic. The sensitivity test is preferably done with a scratch reaction using 10,000 units of penicillin per c.c. of distilled water and taking the reading after 20 mins., when in positive cases definite wheal and flare are seen.

A new compound of benzyl penicillin (i.e. penicillin G) and an antihistaminic amine under the name compenamine have also been introduced for use in such cases (Longacre, 1951). Other newer forms of penicillin have been penicillin O (or allylmercaptyl penicillin G), its repository form chloroprocaine penicillin O and another repository preparation, N:N'-dibenzylethylene diamine penicillin (Fletcher and Knappett, 1953) which has also been used orally (Bayne *et al*, 1953). Penicillin esters have been shown to acquire a high concentration in sputum and lung tissue (Heathecote and Nassan, 1951) but one can possibly produce the same effect by increasing the dosage of soluble or procaine penicillin (Isvael, 1952). However, the high penicillin concentration in cerebrospinal fluid (Schimmel *et al*, 1952) attained after intramuscular injection of neopenil (hydroiodide of diethylaminoethylester penicillin G) may find an application in treatment of meningitis but no such clinical trials have yet been reported. Oral penicillin requires 3 to 10 times the parenteral doses and it is believed to cause sensitisation less frequently. A smaller dosage may be used if it is combined with probenecid (benemid) to delay excretion (Boger *et al*, 1952; Frisk *et al*, 1952). Gastro-intestinal disturbance due to alteration of flora is however more likely to occur with oral therapy.

Repository penicillin is believed to have the greatest advantage in infections accessible to the circulating antibiotic. However, in case of deep seated infections walled off by fibrin or in deep abscess it is more advantageous to raise high blood concentrations by intermittent injections of soluble penicillin (if necessary with probenecid) so that sufficiently high concentration may be attained in the tissue fluid and reach the infected foci (Finland, 1953; Weinstein *et al*, 1951; Eagle *et al*, 1953). This is also applicable to the vegetations in bacterial endocarditis. Here, the choice of antibiotic depends on the micro-organism isolated and its response to antibiotics or their combinations. Large doses of penicillin are usually needed now in this condition possibly due to an increased resistance of these organisms to penicillin. But a combination of penicillin and streptomycin often gives the best results. It is not enough to inhibit growth, the drug must eliminate the last surviving bacteria in the vegetation (Garrod, 1953) and therefore inspite of occasional success with aureomycin, terramycin or chloramphenicol, combinations of antibiotics like penicillin and streptomycin are more likely to be curative (Jawetz and Gunnison, 1950). Since there is an increasing tendency to use higher doses of penicillin in all kinds of infections, it is well to remember that certain organisms show what is known as "zone phenomenon" with penicillin i.e. increasing the concentration reduce the rate of kill of the organisms (Garrod, 1953); Eagle and Mussolman, 1948). This phenomenon, fortunately, does not occur if penicillin is combined with streptomycin. When penicillin is used alone, 2 to 20 times the minimal effective concentration as determined in sensitivity test kill the organisms at the maximal rate (Spicer, 1950).

An advance in streptomycin therapy was thought to be the introduction of dihydrostreptomycin which is, in general, slightly less toxic than streptomycin and has also been sometimes used successfully in patients sensitive to streptomycin. However, it was soon realised that this drug after prolonged use, might cause irreversible damage to the acoustic nerve which is much worse than the slowly reversible changes in the vestibular division produced by streptomycin. So, ordinarily streptomycin remains the drug of choice; how-

ever, the two antibiotics in equal parts are said to minimise the toxicity on either division of VIII nerve.

Aureomycin (chlorotetracycline) and terramycin (oxytetracycline) differ only in the chlorine atom and OH group and a new antibiotic tetracycline has now been prepared divested of these attachments. A variety of streptomyces has also been isolated that directly forms tetracycline. Its advantages are believed to be more stability than chlorotetracycline, lower toxicity (gastro-intestinal) and better penetration of blood brain barrier (Washington Symposium on Antibiotics, 1953).

There is little to choose between terramycin and aureomycin but some individual patients may show greater tolerance to one or the other. Aureomycin may be used in meningitis due to greater access to cerebrospinal fluid in disease condition of meninges (Long *et al*, 1950) whereas terramycin may be preferred in urinary infections. Both are reported to be effective in intestinal amoebiasis (Sodeman *et al*, 1952; McVay and Sprunt, 1952, but possibly they have to be used with other anti-amoebic drugs for the best results (Martin *et al*, 1953). The encouraging results with another antibiotic fumagillin in amoebiasis (Anderson, 1952) could not be confirmed here (Raichaudhuri and Chaudhuri, 1953). Aureomycin, terramycin and chloramphenicol may be used for sulphonamide resistant cases in bacillary dysentery (Garfinkel *et al*, 1953) and Terramycin in oxyuriasis (Loughlin *et al*, 1951).

It appears, that the tuberculostatic effect of terramycin (Steenken and Wolinaky, 1950) may find an important clinical application. When used like PAS the combination with streptomycin it significantly reduced the emergence of streptomycin resistant bacilli at the end of 4 months (Des Antels, 1953). In whooping cough the broad spectrum antibiotics have produced some benefit if administered early (Editorial, *Brit. M. J.*, 1953). They are also likely to provide an alternative to streptomycin in plague therapy (McCrumb, 1953).

The safety or danger of concurrent use of other drugs in antibiotic therapy has to be remembered. Aluminium hydroxide may interfere with the absorption of aureomycin (Beckman, 1952). Cation exchange resin in *in vitro* studies inactivated dihydrostreptomycin immediately and aureo- and terramycin in less than 5 hours but did not affect penicillin or chloramphenicol (Freidman, 1953). The use of anticoagulant with a broad spectrum antibiotic may be risky as the latter would suppress the intestinal flora with consequent inhibition of vitamin K synthesis (Wright, 1952). The administration of ACTH and cortisone besides tending to spread infection may suppress the symptoms and lead to faulty evaluation of the effect of a drug. Penicillin for gonorrhoea may mask the symptoms of syphilis. The disadvantage may be overcome either by giving higher doses as far syphilis or by using streptomycin which however, may readily produce resistant organism (Wilcox, 1951; Lake, 1952).

Controlled observations show that the use of troches of aureomycin, terramycin or procaine penicillin may be followed by various gastro-intestinal disturbance in a high percentage of cases. This, as well as the risks of sensitisation and drug resistance should guard one against its use (Kutscher *et al*, 1953).

The danger of chloramphenicol (probably due to the nitrobenzene radicle) is shown by a number of fatalities reported from aplasia of the bone marrow (Lewis *et al*, 1952; Hawkins and Lederer, 1952) and it is now generally agreed that its use should be restricted to the enteric group of fevers or where the tetracyclines cannot be used profitably. It may be pointed out that inspite of prompt clinical improvement in typhoid fever salmonellae can often be obtained from stools till the sixth week but eventually disappear (Gray, 1953). In contrast chloramphenicol and terramycin sterilise stools of V. cholerae in 1-2 days without any impression on the clinical condition (Chaudhuri *et al*, 1950; Chakravarti *et al*, 1954; Das *et al*, 1951). In treatment of enteric fevers a loading dose is avoided (Chaudhuri, 1948-50; Ramli, 1953). A lower dosage range viz. a daily dosé of 25 mg./kg. by mouth or 50 mg./kg. rectally in one series (Ramli, 1953) and 2 g. on the 1st day and 1 g. daily thereafter in another (Balim, 1950) has given satisfactory results. Complications like perforation and haemorrhage may occur inspite of chloramphenicol treatment and relapse rate may be high. Relapses may be reduced by prolonging therapy (Ramli, 1953) or by simultaneous administration of phenolised TAB vaccine (Sachs, 1951). Salmonella carriers are often refractory to treatment but are likely to respond to chloramphenicol in a dose of 100 mg./kg./24 hrs. for 7 days (Lacore and Conlin, 1953).

Chloramphenicol is in general slightly more active than the tetracyclines against Gram negative organisms and slightly less against Gram positive group. However, its diminished tendency to produce resistant variant (Edwards *et al*, 1952) has left it still a useful drug in some staphylococcal infections that are refractory to penicillin or the tetracyclines. Of the common antibiotics chloramphenicol has the best *in vitro* action in low concentration against different strains of *H. influenzae* (Zinnemann, 1953) and due to its access to cerebrospinal fluid (Long *et al*, 1950) seems to be the drug of choice in *H. influenzae* meningitis (Prather and Smith, 1950; McCrumb *et al*, 1951). Chloramphenicol is largely inactivated in the body and is of little value in infections of the urinary or biliary tract where they appear in active form (Wilson, 1953).

The use of bacitracin, polymyxin and neomycin, due to their nephrotoxicity is mostly limited to oral administration for sterilisation of gut (absorption from which is low) and cutaneous application (Finland, 1953; Church, 1954). However occasionally they have given excellent results on parenteral administration when other antibiotics have failed. The antibacterial spectrum of neomycin is similar to streptomycin whereas polymyxin is chiefly effective against Gram negative rods specially B. pyocyaneus and bacitracin mostly against Gram positive bacteria. Bacitracin alone

(Zendel and Lubart, 1952) or in combination with other antibiotics may be particularly useful in subacute bacterial endocarditis. It has also been used by injection and local application in infections of central nervous system (Teng and Meleney, 1953).

Neomycin, though effective against streptomycin resistant organism has been too toxic for prolonged parenteral therapy. Viomycin also had a similar disadvantage but the use of 2 g. twice a week may be tolerated and produce varying improvement in streptomycin failure (resistant) cases (Editorial, *Brit M. J.*, 1954b).

Synergism and Antagonism of Antibiotics

Combination therapy was resorted to in clinical practice in the hope that two drugs against susceptible organism would act better than one. While this happened in many cases, sometimes the combined efficacy was reduced. This led to a closer study of the effect of different combinations of antibiotics and to an important observation that combinations of antibiotics or other chemotherapeutic substances may delay the emergence of resistant strains. A well known example of this is the combination of streptomycin with p-amino salicylic acid (M. R. C. Rep., 1949) or iso-nicotinic acid hydrazide (M. R. Council Rep. 1953). The effect of combining an antibiotic or antibiotics with sulphonamide to delay resistance to organisms has been reported (Carpenter *et al*, 1945; Kaipainen, 1951; 1952).

The indications for combined therapy may be Garrod, 1953): (i) mixed infections, (ii) prevention of acquired resistance, (iii) prevention of toxic effects and (iv) urgent undiagnosed case. The use of "sulphatriad" to prevent crystalline deposit in urine while maintaining efficacy and a reduction in the dosage of streptomycin by combination with other drugs or antibiotics illustrate that combinations may effect reduction of toxicity. Combined therapy in undiagnosed cases to cover a wide range is to be deprecated as this obscures the diagnosis but may have to be used in case of urgency after collecting materials for bacteriological examination. To the list mentioned above may be added infections not responding well to single antibiotics but yielding to combinations—synergistic action.

The question of synergism and antogonism has been extensively studied *in vitro* and the complexity of the problem will be realised from the fact that the same combination may act synergistically with regard to one organism and antagonistically to another (Jawetz and Gunnison, 1952). Besides, the proportion in which the two antibiotics are combined may also determine whether there would be synergism or antagonism (Price *et al*, 1949). However the work of (Jawetz *et al* 1952) has led to some general rules which would indicate the behaviour of a group of antibiotics in treatment. They have classified the more common antibiotics into two groups: (1) penicillin, streptomycin, bacitracin, neomycin (bactericidal); (2) aureomycin, terramycin, chloramphenicol (bacteriostatic). The drugs of the first group act synergistically to one another and do not show antagonism between themselves; drugs of the second group show neither synergism nor antagonism but may be simply additive. A combination of members of the two groups is usually antagonistic, the antagonism being against the bactericidal drugs. The bacteriostatic action probably inhibits the metabolic processes of growth necessary for the action of bactericidal drugs (Brownle, 1952). But if the organism is selectively resistant to the member of the first group and somewhat susceptible to that of the second, their combination may yield synergistic results. This explains the occasional success of combinations like terramycin plus streptomycin and penicillin plus aureomycin (Jawetz *et al*, 1951a; Spies *et al*, 1951). The usual antagonism of the drugs in question in case of sensitive organisms has been demonstrated in experimental animals and clinically with different combinations (Speck and Jawetz, 1952; Jawetz *et al*, 1951b; Lepper and Dowling, 1951). Put possibly host response, phagocytosis and other factors play a part, for, while there was an antagonism between penicillin and aureomycin in pneumococcal meningitis (Lepper and Dowling, 1951) no such interference was seen in pneumococcal pneumonia (Ahern and Kirby, 1953). This is also indicated by a high efficacy of the combination terramycin plus streptomycin in brucellosis (Magill and Killough, 1953). Sulphonamide and penicillin in combination may produce an enhanced effect (Bigger, 1944) which is considered successive and complementary action of the two drugs, penicillin reducing the number of bacteria to a level where sulphonamide may exert its full effect (Garrod, 1953). The clinical results with streptomycin and sulphadiazine in brucellosis (Spink *et al*, 1948; Scowen and Garrod, 1948) and plague (Wagle and Bedarkar, 1948) and of penicillin and sulphadiazine in pneumococcal meningitis (Waring and Smith, 1944; Smith *et al*, 1946) are confirmatory.

Microbial Resistance to Antibiotics

This is a complicated and disturbing problem of antibiotic therapy. The organism may be naturally resistant e.g., some strains of streptococcus or staphylococcus or it may remain sensitive at the beginning and only acquire resistance during its exposure to the drug. The mechanism of development of this resistance may be explained by adaptation or mutation (Hinshelwood, 1944; Demerec, 1945). The subject is controversial (Abraham, 1953) and an ingenious method of mutation of B. coli to streptomycin resistant type in the absence of streptomycin (Lederberg and Lederberg 1952) tend to support the latter view. Another technique of developing resistance has been growing organisms in presence of desoxyribonucleic acid obtained from strains made resistant by exposure to the antibiotic (Avery *et al*, 1944). It is considered that biochemically deficient mutants occur naturally or a normal minority is kept under some inhibitory influence exerted by the majority (Pratt and Dufrency, 1949). These may take

the lead in growth and multiplication when the sensitive organisms are eliminated. All resistant organisms do not produce enzymes to destroy the antibiotic (the production of penicillinase by some bacteria is a well known example of this) but differ in their biochemical behaviour. The resistant organisms probably successfully bypass the metabolic pathway blocked by the antibiotic. This also explains the delayed development of resistance with two drugs which can attack at two different points in the cell metabolism. An interesting observation has been recovery of sensitive mutants from resistant organism (Barber, 1949). Penicillin sensitive organisms from resistant strains have been obtained by culture in penicillin free medium (Gotts, 1945) or in contact with another organism (Voureka, 1948). Besides organisms made resistant against one antibiotic (neomycin) have been rendered more sensitive to others (tetracyclines) (Gocke and Finland, 1951). Exposure to aureomycin *in vitro* has also led to suppression of penicillinase production by penicillin resistant staphylococci which may thus be rendered sensitive to penicillin (Chandler and von der Goltz, 1952). The clinical possibilities of these findings are yet to be seen (Dowling, 1953).

The development of resistant to streptomycin occurs in rapid stages whereas with other antibiotics it is a slower process. Though penicillin resistance has been worked up *in vitro* (Miller and Bohnhoff, 1947; Sesler and Schmidt, 1942) its use in therapy has been relatively free from the emergence of resistant variants apart from staphylococci. The microbial resistance is usually specific for the antibiotic to which the organism is exposed but cross resistance may develop between chemically related substances like aureomycin and terramycin and less often between the tetracyclines and chloramphenicol (Gocke and Finland, 1951; Jawetz *et al*, 1951b; Jawetz *et al* 1951c).

Some organisms again may become actually dependent on the antibiotic for their growth. This was first reported with streptomycin (Miller and Bohnhoff, 1947b) and strains of tubercle bacilli showing this property have been isolated (Miller and Bohnhoff, 1949).

Effect of Antibiotics on Balance of Microbial Flora

The use of one antibiotic in a mixed bacterial population may, by suppressing the sensitive bacteria, lead to an unbriddled growth of the insensitive organisms. These not only multiply in high concentration of the antibiotic but organisms which are normally non-pathogenic may, by their abundant growth, produce pathological effects. It is well known that the administration of penicillin may be followed by a marked increase of the Gram negative organisms (Somner and Favour, 1949). Similarly the administration of streptomycin has been followed by bacterial infections by staphylococcus aureus or other resistant organism (Weinstein, 1946; Weinstein, 1947). But a more serious state of affairs has been brought about by the indiscriminate use of the broad-spectrum antibiotics aureomycin, terramycin and chloramphenicol which may cause unrestrained growth of insensitive bacteria and fungi like proteus vulgaris, pseudomona aeruginosa, cryptococcus, aspergillus, staphylococcus aureus, klebsielle pneumoniae, candida albicans (Barach *et al*, 1952).

Yow (1952) has stressed the importance of proteus and pseudomonas infection during antibiotic therapy and cites cases of surgical wound where the antibiotic had to be withdrawn and normal flora re-established before immunity developed. In three cases, septicaemia or empyema due to these organisms ended fatally. He found polymyxin B effective for pseudomona and streptomycin and sulphonamide for proteus infection. Overwhelming growth of insensitive organisms in treatment of pulmonary suppuration may end fatally. As a precaution it is recommended that the use of these antibiotics in such cases be limited to a short period if required and penicillin by inhalation given to raise the concentration if the organisms are ordinarily insensitive (Barach, *et al*, 1952). Repeated sputum cultures should be done for selective chemotherapy and for detecting predominance of organisms like proteus, monilia etc. after treatment is commenced.

The intestinal flora undergoes profound changes following administration of the broad spectrum antibiotics with elimination of most of the bacteria and consequent reduced biosynthesis of vitamins. Both these —the former by unchecked growth of fungus and the latter by reducing resistance to host (Harris, 1950)— may lead to moniliasis of the gastrointestinal tract or lung. A case of uraemia due to blockage of ureters by fungal growth following chloramphenicol therapy has been described (Taylor and Rundle, 1952). In this connection a recent report of the efficacy of undecylenic acid in preventing the monilial complications (Mountain and Krumenacher, 1953), if confirmed, will be of great interest. A peculiar form of anorectal pruritus, burning and erythema, sometimes caused by the broad spectrum antibiotics (Manheim, 1951) may also be due to the alteration of flora or a change in pH. Changes of bacterial flora following erythromycin is less drastic, the Gram positive organism being chiefly affected and monilial overgrowth is not likely to occur (Tice, 1953).

Antibiotics and the Liver

The efficacy of certain antibiotics in reducing or delaying hepatic necrosis of rats on a necrogenic diet has been demonstrated. Aureomycin is most potent in this respect but a few other antibiotics (e.g., terramycin, streptomycin) are also effective (Gyorgi, 1951; Gyorgi *et al*, 1951). It is not certain how the beneficial effect on the liver is exerted but the available evidence suggests an inhibition of bacterial flora and toxic absorption from the lower intestine (Gyorgi *et al*, 1950). A lipotropic action of aureomycin has also been demonstrated in rats kept on high fat, low protein, choline free diet (Gyorgi, 1952) or dogs with impaired pancreatic function (Kaplan *et al*, 1954). It is doubtful

if urinary choline excretion (as trimethylamine) is diminished by aureomycin through its action on intestinal bacteria (Kaplan *et al*, 1954; De La Heurga and Popper, 1952). The effect is more likely to be related to vitamin B_{12} and folic acid (Stockstad, 1954).

Clinical trials of aureomycin in chronic liver diseases have given encouraging results (Kalz, 1947; Knight, 1949) and some spectacular recoveries from hepatic failure have occurred (Chura, 1951; Conti and Cassana, 1949; Kimbrough, 1951) In infective hepatitis variable results have been reported (Felsenfeld *et al*, 1950; Desmont, 1951; Kaminska and Szaflarski, 1950), but possibly the more severely ill cases are benefited (Hanso and Simrock, 1949).

However some other reports sound a note of caution in the use of aureomycin in liver diseases. Aureomycin in a high dose parenterally (75-150 mg./kg.) or orally (320-400 mg./kg.) has been shown to produce toxic effects on the livers of mice. Similar changes were also seen after intravenous administration in dog (Lepper *et al*, 1951b) and man (Lepper *et al*, 1951a; Rutenberg and Pinkes, 1952; Bateman *et al*, 1953) and it is recommended that in case of parenteral aureomycin therapy the total daily dose should not exceed 2 g.

Antibiotics in Radiation Sickness

One of the recent applications of antibiotic therapy is in radiation injury caused by x-rays, radium or atomic energy. Antibiotics have protected animals exposed to lethal dose of radiations (Miller and Hammond, 1950; Atomic Energy Comm. 1951; Rambert, 1950) and aureomycin has given better results than penicillin streptomycin and chloramphenicol (Howland *et al*, 1949). They probably act by inhibiting sepsis, since radiation tends to produce a systemic invasion by micro-organism through the damaged mucous membrane of the gut (Miller and Hammond, 1950; Hammond and Miller, 1950) and depresses the bone marrow and reticulo-endothelial cells with consequent leucopenia and suppression of immunity response.

In acute radiation syndrome of atomic energy workers or victims antibiotics have been found to be the only agents of definite value in treatment and prophylaxis (Hempelmann, 1951). This however does not preclude the use of other supportive measures like blood transfusion, adequate protein intake etc. In radiation sickness pyridoxin and hydrochloric acid have also given good results (Ellis and Stoll, 1952) and ACTH has been favourably reported (Taber, 1951).

Antibiotics in Shock

Some experimental findings (Fine, 1953) suggest that antibiotic may be of value in the treatment of shock. Pre-treatment with aureomycin, terramycin, penicillin or neomycin in dogs subjected to haemorrhagic shock prevented irreversible changes and increased the final survival rate from 21 per cent to 65-85 per cent. Streptomycin also had some effect while chloramphenicol, bacitracin and sulphonamide were ineffective. The drugs were given orally or in case of penicillin by duodenal tube. Neomycin and aureomycin when given by portal vein were also effective. It is not yet certain whether the action of the antibiotic was due to antibacterial or pharmacological effect. The growth of aerobic and anaerobic organisms from liver and blood of the dogs suggested antibacterial action preventing multiplication of the organisms from intestine in hypoxic tissues. But the increased survival of dogs in haemorrhagic shock at 36 hours with "inactivated" aureomycin and the successful treatment of shock in rats which are not prone to bacterial invasion of tissues (Baez, 1953) suggest a pharmacological action. Whatever may be the mechanism, there was no doubt about the efficacy of the drugs in saving the animals from the effects of shock. If these results are applicable to man, it will open an important therapeutic field.

Nutritional Effects of Antibiotics

The effect of the antibiotics in animal nutrition has been extensively studied and a growth promoting action observed with most of the antibiotics (Stockstad, 1954, Williams, 1953). The growth effect in chicks is produced by aureomycin, terramycin, penicillin, streptomycin and bacitracin in very minute amounts in diet (1 to 20 parts per million). The effect in other species of animals may vary with the antibiotic used but most consistent results are likely to be obtained with the broad spectrum antibiotics. The experimental evidences point to an action on the intestinal micro-organisms (Moore *et al*, 1946; Coates, 1954) rather than a direct metabolic effect (Weber, 1952). Animals reared in a relatively bacteria free environment have shown increase rate of growth which could not be improved by addition of antibiotics (Coates *et al*, 1952; Reyniers, 1950; Cuthbertson, 1952). The effect of parenteral antibiotics is weaker and depend on their excretion in stomach and intestine (Elam *et al*, 1951; Cole, 1953), while the poorly absorbed preparations (streptomycin, bacitracin) may be quite active. The other effects viz. reduction in the weight of the intestine and improved absorption of vitamins and minerals are also seen in the "germ-free" animal and suggest that the antibiotics act by preventing a low grade infection and perhaps an "early sprue-like" condition (Williams, 1953; Coates, 1954; Gordon, 1952). This would also explain the better response obtained in animals kept in insanitary conditions or in a state of subnormal nutrition and the improvement in the utilisation of food and the sparing effect on proteins and certain minerals and vitamins (Stockstad, 1954).

Limited clinical trials in children with aureomycin (50-150 mg. daily for 1-3 years) show increased rate of growth with a marked absence of gastrointestinal upsets (Serimshaw, 1953). Its use in premature infants has been followed by improved weight gain and reduced morbidity and mortality (Perrini, 1951; Snelling and Johnson, 1952; Robinson, 1952). However proper clinical assessment is difficult without more experience.

Aureomycin has prolonged the life of rats rendered anaemic by formation of intestinal diverticula (Watson and Witts, 1952). It may also counteract the toxicity of aminopterin in rats (Waisman *et al*, 1951) though reports are variable (Sauberlich, 1953). There has been a few reports (Litchman *et al*, 1950; Foy *et al*, 1951) of cases of pernicious anaemia responding to antibiotics (aureomycin, penicillin) but this has not been uniformly observed (Ungley, 1950). It is postulated that the effect may be due to a change of bacterial flora which make vitamin B_{12} and folic acid more available to the patient (Litchman *et al*, 1950) or to the reduction of bacterial production of some inhibitory factor (Callender and Lajtha, 1951).

Some antibiotics inhibit protein and nucleic acid synthesis. An antibiotic with a selective application of this property would be useful against tumours (Editorial, *Brit. M. J.*, 1954a). Such an effect has been observed with actinomycin C (Waksman, 1953) and more recently with L-azaserine which has a notable action on transplanted mouse sarcoma (Bartz *et al*, 1954; Stock *et al*, 1954).

Future Development

Though most of the bacterial infections have been brought under control by antibiotic therapy fungus and virus infections have practically remained unresponsive apart from some actinomyces and a few larger viruses. Experimental work, however, has already raised hopes that antibiotics effective against fungus (Senena *et al*, 1952; Hickey *et al*, 1952) and virus (Shope, 1953) may still be discovered. Research in antibiotics is further stimulated by the phenomenon of drug resistance which threatens, with time, to render most of the currently available antibiotics ineffective and newer ones will have to be found if continued efficacy even in bacterial diseases is to be maintained.

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CASE NOTES

NECROPSY FINDINGS IN YELLOW OLEANDER POISONING

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The Madras Chemical Examiner's reports for the years 1946-49 and 1951 record 18·9 per cent of human poisoning with oleander in 907 organic poisons detected for the period. Oleander is commonly used as suicidal poison and occasionally administered with the intent to murder in our country. The white, pink and yellow oleander are common garden plants. All parts of the plant are poisonous. The active principles contained in them in comparatively small dose are highly toxic to the heart and spinal cord and invariably prove fatal. The glycosides of oleander rapidly hydrolyse and decomposition of the cadaver promotes rapid hydrolysis and destruction of the glycoside. This often accounts for the inability to detect oleander glycosides in the viscera in clinically recognised cases of oleander poisoning. These features made oleander a favourite poison. But scant mention is made of the postmortem findings in oleander poisoning and remarks like "Necropsy findings not characteristic" in oleander poisoning are recorded in books on toxicology. This has encouraged us to record the clinical and necropsy findings in a case of yellow oleander poisoning.

CASE REPORT

CLINICAL FINDINGS:

At 3 p.m. on 10-9-1953, a male named S. P., aged 30, in perfect health consumed the powder of 3 yellow oleander seeds. He soon developed abdominal pain and vomiting. On admission to the King George Hospital, Visakhapatnam, he was found to be restless and complained of extreme thirst. Pulse was imperceptible. Heart rate was 50 per minute and a considerable number of beats were found missing. Blood pressure could not be recorded. Urine showed no abnormality. Lungs were clear. Abdomen was tender all over but not rigid. Tongue was dry. Pupils were of normal size. Temperature was subnormal.

At hourly intervals he was given twice 2 c.c. of coramine and 100 mg. of vitamin B. At 12 noon he was cold and clammy. The heart beats were feebler and 70 per minute. Blood pressure 66/30? mm.Hg. Intravenous glucose saline with coramine was administered. At 2 p.m. the heart rhythm was irregular and the general condition was poor. His mind all the while was clear. Prior to death at 3-15 p.m. ventricular fibrillation set in.

MAIN NECROPSY FINDINGS INCLUDING HISTOLOGICAL OBSERVATIONS (P.M. No. 264):

Heart—The heart was soft and flabby. It weighed 280 grammes. Multiple subpericardial petechiae, some

of them confluent were seen over the posterior surface of the ventricles and the area bordering the auriculo-ventricular junction (Fig. 1, *vide* Plate). Massive subendocardial haemorrhages of the right ventricle were observed (Fig 2, *vide* Plate). Sections of heart studied from three paraffin blocks revealed extensive but patchy areas of haemorrhagic necrosis of myocardium of varying grades of severity. In some places total destruction of muscle fibres was observed while in other places carcinoma was only left over to hold the collections of red blood cells; result of haemorrhagic necrosis of muscle fibres (Fig. 3, *vide* Plate). The myocardium adjoining subpericardial petechiae showed extensive haemorrhagic necrosis and the surviving muscle fibre bundles were separated by columns of red blood cells (Fig. 4, *vide* Plate). The surviving strips of myofibrils were surrounded by sheets of haemorrhage (Fig. 5, *vide* Plate). The subendocardial haemorrhage had swept through the myocardium and extensive haemorrhagic necrosis of the myocardium adjoining the endocardium was observed (Fig. 6, *vide* Plate). Collections of haemosiderin pigment and mononuclears were seen at the haemorrhagic areas.

Lungs—Subpleural petechiae and mild degree of oedema observed.

Liver—Weighed 1600 grammes. Congestion and dilatation of the sinusoids noticed.

Kidneys—Massive intertubular haemorrhages of the medulla.

Brain—Weighed 1600 grammes. Congestion of meningeal and cortical vessels seen.

The chemical examiner detected no oleander or any other poison in the stomach, intestines and their contents, liver, kidney and the urine.

Comments

The clinical history and findings and necropsy observations are characteristic of oleander poisoning. The clinical and necropsy findings indicate the necrotising action of the glycoside, thevetin, contained in the yellow oleander ingested by the deceased. The absence of oleander in the viscera submitted to chemical examiner may be due to the poison being mostly lost in the repeated vomitings and the small quantity remaining was lethal enough but was excreted during the 24 hours the patient survived. Unlike digitalin, thevetin is excreted rapidly. Dr. P. Venkatarao, Chemical Examiner, Government of Madras, is of the same opinion. The total absence of symptoms pointing to spinal cord affection in the deceased is significant. The pancardial haemorrhages observed should caution clinicians when subjecting patients to heroic doses of digitalis, for digitlis and oleander glycosides possess identical pharmacological action.

Acknowledgment

With pleasure we acknowledge the services rendered by photo-artists Edwin and his son.

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UNILATERAL BRONCHIECTASIS DUE TO ASPIRATION OF A FOREIGN BODY

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Bronchiectasis is a fairly common condition. The condition is now-a-days more frequently recognised on account of the improved methods of investigations like bronchoscopy and bronchography and also due to the awareness of the fact that a congenital bronchiectatic state may remain unrecognised for a long time owing to the absence of clinical manifestation later recognised after years of silent existence due to some pulmonary infection brought on by the aspiration of a foreign body and subsequent bacterial infection. The outlook on recovery from this condition has considerably improved owing to improved methods of effecting drainage and to newer operative measures such as, lobectomy, pneumonectomy, total or segmental.

The following is the record of a case which recently came under our observation.

Case Report

P. Venkataswami, male, 42 years old, shopkeeper by occupation, was admitted in the Victoria Hospital, Bangalore, on 13-9-1953. He gave a history of cough, with foul smelling expectoration, irregular fever and pain in the right side of the chest for the preceding eight months. The previous history was that about 8 months ago he had an attack of fever and headache, and he was advised by a friend to suck the juice of betelnut at bed time to allay thirst. Accordingly, he used to keep a full-sized betelnut in his mouth while going to bed. One day in the early morning, he suddenly woke up with a severe bout of cough. From that time onwards, he suffered from paroxysmal attacks of cough and developed irregular fever about a month later.

He went to a hospital for treatment, where he was thought to be suffering from pulmonary tuberculosis and was advised to take a course of streptomycin injections. He took those injections after which the fever subsided. But the cough and pain in the chest persisted. He went to another hospital where he was put on streptomycin, calcium and sulphanilamides for further two months. He felt considerably better and the paroxysmal cough was diminishing. He returned to his native place and after 5 months' stay there all his original complaints, i.e., fever, cough, pain in

Fig. 1—Illustrates subpericardial petechiae, some of them confluent, over the posterior aspect of ventricles.

Fig. 2—Illustrates massive subendocardial haemorrhage of the right ventricle. Fine line of separation between the ventricular muscle and endocardium caused by the intervening haemorrhage is seen.

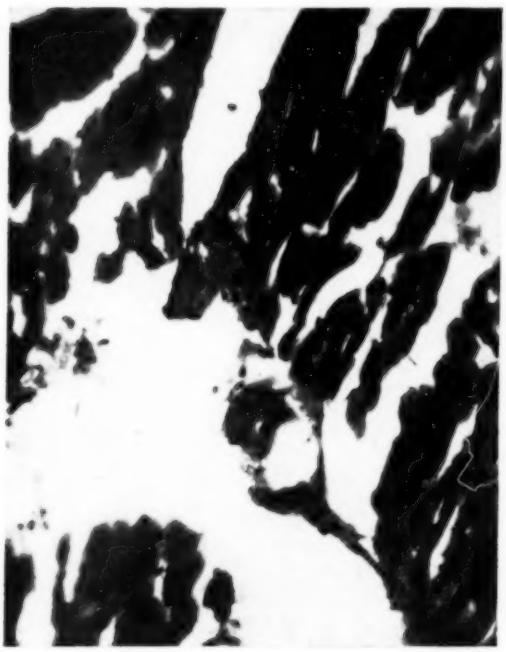

Fig. 3—Illustrates haemorrhagic necrosis of myocardium. All that is left of the terminal part of muscle bundle is sarcolemma enclosing red blood cells (H & E × 100).

Fig. 4—Illustrates massive subpericardial haemorrhage and haemorrhagic necrosis of myocardium. Columns of red blood cells are seen to split the muscle bundles (H & E × 100).

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Fig. 5—Illustrates extensive myocardial haemorrhagic necrosis and haemorrhage. The surviving muscle bundles show fragmentation and cloudy swelling (H & E×100).

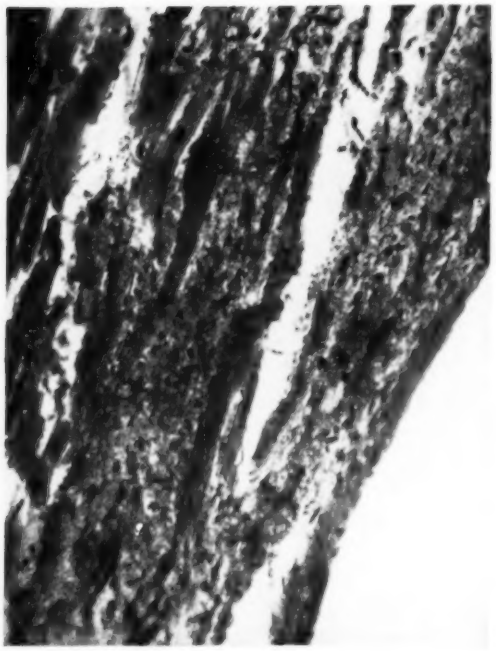

Fig. 6—Illustrates subendocardial and myocardial haemorrhage. The surviving muscle bundles are widely separated by sheets of haemorrhage (H & E×600).

REDDY AND RAMASUBBARAO—*Necropsy Findings in Yellow Oleander Poisoning (pp. 559-60)*

Fig. 1—Skiagram taken on 14-9-53

Fig. 2—Expectorated Foreign Body (actual size)

Fig. 3—Skiagram taken on 21-10-53

PUTTAIYA AND JANARDHANA—*Unilateral Bronchiectasis due to Aspiration of Foreign Body (pp. 560-61)*

the chest and foetid expectoration set in again and he sought admission into Victoria Hospital for treatment.

On examination, he was found much emaciated and had moderate anaemia. There was no clubbing of the fingers. The respiratory excursions on the right side were diminished. The intercostal spaces at the base of the chest on the right side, were drawn in. There was suspicion of inspiratory retraction over this area. Percussion note was mildly impaired and leathery rales were audible over this area, particularly on the posterior aspect while R.M. and V.R. were considerably diminished.

A radiogram of the chest (Fig. 1, *vide* Plate) was taken and a diagnosis of unilateral bronchiectasis was made. The sputum was repeatedly examined and was found to be negative for acid-fast bacillus.

He was put on a course of penicillin-streptomycin combination injections and sulphadiazine tablets orally The fever subsided within a few days and the patient also improved subjectively except for his cough and foetid expectoration. Postural treatment was then adopted and he was made to sleep on his left side with the foot of the bed elevated. This procedure brought about improved drainage. On 18-10-1953, the patient got a severe bout of cough while taking his bath and coughed out a large quantity of thick foul smelling sputum and in it was found a globular mass of the size of a betelnut which he preserved for inspection (Fig. 2, *vide* Plate). After this event the patient made a dramatic recovery. A control radiogram (Fig. 3, *vide* Plate) showed a satisfactory clearing up of the lung lesion. He was discharged from the hospital on 26-10-1953 completely relieved of his complaints.

INVESTIGATIONS—The following investigations were made:

Blood—Erythrocytes per c.mm.—4·2 million; Haemoglobin (Sahli)—85 per cent; Leukocytes per c.mm.—12,800: Poly.—80 per cent, Lympho.—16 per cent, Mono.—3 per cent and Eosino.—1 per cent.

Blood for W.R.—negative.

Urine—No abnormality.

Sputum—Streptococci, staphylococci and pus cells found. Tubercle bacilli—not found (even after examining the sputum consecutively for six days).

Radiogram of the Chest—A skiagram taken on 14-9-53 (Fig. 1, *vide* Plate) showed bronchiectasis mostly confined to the right side. Another skiagram was taken on 21-10-53 (Fig. 3, *vide* Plate), 4 days after the expulsion of the foreign body.

DISCUSSION

Aspiration of a foreign body and its impaction in the glottis, trachea and bronchi are fairly frequent accidents according to the report of Asherson (1953). Impaction results from a sudden deep full inspiration there being no reserve of air in the lungs to expel the intruder. When a foreign body lodges in a main bronchus and obstructs its lumen completely the clinical signs are those of an atelectasis. If the obstruction is of the ball-valve type trapping in more and more air with each inspiration, the signs are those of an obstructive emphysema. Asherson (*loc. cit.*) advocates taking the x-ray pictures of the lungs at the height of expiration and inspiration during radiological investigation as the uniformly dark lung shadow remains unaltered throughout the respiratory cycle and the diaphragm persistently elevated in the case of atelectasis when the heart is drawn towards the side of lesion while in obstructive emphysema the heart and mediastinal shadows are pushed over to the opposite side and the lung remains (hypertranslucent in both inspiration and expiration and the cupola of the diaphragm flat and depressed with restricted movement in the different phases of respiration. In the case quoted by us the heart was pulled to the right side and there was irregular opacity over the right base. Perhaps the F.B. had got impacted in one of the segmental bronchi over the right base and had caused collapse of this segment, subsequent infection, enzymatic digestion, liquefaction and expectoration of the liquefied material had released the F.B. from its impaction and the F.B. thus released had been expectorated out in one bout of cough. It is a wonder the patient did not suffer from any severe asphyxial symptoms at the time he aspirated the nut and sought medical advice after the lapse of one full month when only pain and fever set in, for, Asherson (*loc. cit.*) mentions "Death, delayed but inevitable, also follows if a main bronchus becomes blocked". When the foreign body causing impaction is not radio-opaque radiological examination will not help us to clinch the diagnosis as to the cause of this obstruction whether it is a neoplasm or a foreign body. Bronchoscopy may help us to tide over this difficulty. We also, were unable to establish the presence of a F.B. as we could not do a bronchoscopy though we suspected some such cause as the patient gave the history of having kept an arecanut in his mouth and after getting an attack of cough of not finding this nut in his mouth. Time helped us to establish the diagnosis as with passage of time and increasing liquefaction of lung tissue around the F.B. this body was freed and expectorated out.

Two aspects of the case stand out as pointers to us for our future guidance in our responsibilities towards patients who come to us with unilateral bronchiectasis of sudden onset. One is correct history taking. If the patient had given a correct history of having aspirated an arecanut or the aspiration of a foreign body had been suspected earlier he could have saved himself months of suffering and unnecessary expense. Secondly, routine bronchoscopic examination, wherever pissible, will help to elucidate the aetiological basis of many an obscure case of unilateral bronchiectasis.

ACKNOWLEDGMENT

We are grateful to Dr. M. Guru Das of the x-ray department, and Dr. K. V. Ghorpade of the pathology department for their valuable assistance in our investigations of the above case, and to Mr. R. Raju, technician, x-ray department, for the photographs.

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JOURNAL OF THE
INDIAN MEDICAL ASSOCIATION
CALCUTTA, SEPTEMBER, 1954

CYTOLOGY AND CYTOCHEMISTRY OF PROTOZOAN PARASITES OF MAN

The science of cytology aims at comprehensive knowledge of the morphology of the cell, its chemical constitution, physical or physicochemical character, the functions of its nucleus and the various cytoplasmic structures and constituents. How the complex processes of metabolism are carried out, the influence of its environments, problems of reproduction and genetics, how the morphogenesis of an organism takes place from a single fertilised cell and what chemical or enzymic factors determine this process,—all these and other problems dealing with the mysteries of the process are the subjects of investigation of the cytologists.

About the beginning of the present century, as the result of work of the pioneers of histology, a fair idea as to the morphology of cells as seen in fixed tissue specimens was obtained and it was known that there were two types of nucleic acid which were regarded as characteristic of animal and vegetable cells, viz., thymus nucleic acid which was obtained from the thymus gland and yeast nucleic acid respectively.[1] These nucleic acids have now come to be known as desoxyribonucleic acid (DNA) and ribonucleic acid (RNA) and are found in both animal and vegetable cells, the former being found predominantly in the nucleus and the latter in the cytoplasm. Even thirty or forty years ago the science of cytology was concerned chiefly with the morphology of cells, its nucleus and chromosomes and their role in reproduction and genetics. With the advance of investigative technique limitations of studying fixed specimens gradually became apparent and for about a quarter of a century since 1910, great stress was laid on the study of the living cell and experimental cytology. Some phenomena of life process could be analysed and physicochemical processes involved could be understood so that working hypotheses regarding specific cytochemical organisations in particular parts of cells could be postulated. Further advance was brought about by the development of certain cytochemical methods by Feulgen, Caspersson Gomori and Takamatsu, Linderstrom-Lang and Holter and others.[2] Modern cytochemical methods are constantly being improved and tested for accuracy of localisation and certain physicochemical forces coming into play during cytochemical processes which might render the results unreliable. Inspite of the fact that there exists considerable difference of opinion among various workers—a feature that is inevitable and natural in the process of growth of a new science—regarding the validity of certain cytochemical methods[3, 4] and the interpretation of the results obtained by various studies, this branch of cytology has provided considerable insight into the chemical constitution of the different structures in the cell and their functions. At the present time the science of cytology employs besides older histological methods, newer methods of cytochemistry, microanalysis, microdissection and study of living cells, measurement of cell metabolism, newer methods of optics and physics, viz., phase contrast and electron microscopy, utraviolet fluorescent microscopy, ultraviolet microspectrophotometry, use of radioactive isotopes and various other biochemical and physicochemical techniques[5, 6]. In view of the highly specialised nature of these techniques, which it is practically impossible for a single individual to master in his life time, entire teams of workers having specialised training in these methods, have to work on individual problems.

Most of the cytological investigations that have been carried out during the last twenty-five years have been on the metazoan cell and some free living protozoa. A metazoan cell is an individual in a community having specialised functions and affected considerably by the activities of other cells in the organism, the results of which reach it through the humors passing to its internal environment, the *milieu interieur*, or intra-organic medium. Consequently the life process is very specialised and complicated. The protozoon, on the other hand, is the entire organism itself. Its physiological activities originate mainly in itself as the result of stimuli or chemical processes taking place in it, though it is affected in different phases of its life by its external environment as well. It is thus probable that study of this single unit of life process may yield information of fundamental importance.

Cytological study of protozoa is however beset with some difficulties which are intrinsically due to the nature of the protozoa themselves. Most protozoa cannot be readily cultivated in the pure state in artificial media and cultivation takes relatively longer time in comparison to bacteria. This is apparently responsible for the relative paucity of cytological investigations on protozoa, particularly of the protozoan parasites of man. There have been excellent investigations carried out on the nutritional requirements and metabolism of certain parasitic protozoa, viz., those belonging to the family *Trypanosomidae*, certain plasmodia, and *Entamoeba*

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histolytica.[7] But the literature on the cytochemistry of protozoan parasites of man is distinctly meagre. A paper on the cytology of the parasite of kala-azar was published last year[8] and the present number includes another on the cytochemistry of *E. histolytica*.[9] A number of papers on the cytology of certain plasmodia have also appeared during the recent years from this country,[10, 11] and abroad[12, 13, 14]. These papers provide newer knowledge as to the chemical constitution of these parasites and some idea as to the physiological activities and cytochemical changes that occur in different phases of their life or functional activity and environmental conditions.

The importance of cytochemical study of protozoa that infect man, lies in the fact that it may help in the solution of many problems in host-parasite relationship in addition to providing an insight into the mechanism of physiological activities of these organisms. What actually is the chemical constituent that enables the parasite to survive the natural defence mechanism of the host on its entry into man, how it adapts and invades the host tissues, what chemical changes occur as the result of immunity reactions, of drug action, how the parasite acquires drug resistance—valuable information may be obtained on these problems by cytochemical investigations. Knowledge of nutritional requirements. enzyme systems, mechanism of drug action, may well be utilised to evolve effective compounds against these parasites as against certain bacteria and malignant cells, e.g., aromatic diamidines against the protozoa of the trypanosome family, isonicotinic acid hydrazide against the tubercle bacillus, anti-folic acid compounds against acute leukaemias, etc.

Histochemical study of the changes that occur in the host as the result of parasitic infection may show the changes that occur in the tissue cells, e.g., in enzyme distribution, content of various carbohydrate, lipids and proteins in the cell, or those that occur in the nucleus and cytoplasm, may provide characteristic pattern of changes in organs likely to be of value in diagnosis.

Cytology and cytochemistry are rapidly developing sciences and full of promise. Application of these to protozoa and protozoan diseases should be encouraged in this country where these diseases take a considerable toll of human life. Fundamental knowledge that may be applied to alleviation of human suffering may result from such investigations.

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STUDENTS' HEALTH—A PROBLEM

A physical checkup of 4674 boys and girls of the primary schools of Calcutta Corporation recently done, reveals that only sixteen per cent of them possess what might be called normal health. The rest have got either some specific ailments or disorders which are certainly devitalising.

A sample survey of the health and living conditions of the undergraduate students of the Calcutta University initiated by the Vice-Chancellor, was also conducted lately. This too has brought to light a very gloomy picture of the present state of health and living conditions of the younger boys and girls of our country. According to this survey, eight out of ten students in Calcutta complain of some physical ailment or distressing symptoms. Thirty-one per cent of the students live on "below subsistence diet" and fifty-five per cent live in the average floor space of near about twenty-four square feet which is "just sufficient for a cot or a charpoy of good size". And these are factors which no doubt do not contribute to positive health.

The results arrived at in these surveys at Calcutta are not an isolated phenomenon. This picture holds good in any part of the country and is a pointer to the national crisis it may lead to, in course of time.

Children determine a nation's future. Health in the early years of life shapes the later frame, physical and mental. An emaciated and diseased child seldom grows into a healthy and virile life. The protection of the child from infancy to adolescence should be the concern of the State.

It is needless to point out that the State can have no more valuable assets than physically and mentally healthy children. An immediate and thorough investigation has become necessary to find out the causes of this general deterioration of health amongst the younger folk of our nation.

Undernourishment has been held responsible for much of this state of affairs. Really the finance of the people has in the present time become so slender in contrast to the prevailing high prices of all essential commodities that arrangements for adequate nutrition of children cannot be expected from most of the families which constitute the bulk of our society.

Medical men in the present situation are constantly drawing the attention of the Government to the health of the children. Arrangements for free and wholesome tiffin in schools and regular physical checkup as suggested by the Indian Medical Association all over India might improve matters to some extent. Preventive medicine which has now become a regular programme in every country cannot work well with people who lack adequate nutrition. The problem is a socio-economic one and cannot be solved by individual efforts. The State, the medical profession and the public should immediately combine to better India's nutritional status, especially of the child.

CURRENT MEDICAL LITERATURE

ERYTHROMYCIN

HERRELL (*Practitioner*, **172**: 316, 1954) gives in the following the summary of his observation:

Erythromycin is a penicillin-like antibiotic. It is primarily an antibiotic to be administered by the oral route.

Erythromycin is highly effective in the treatment of infections with micro-organisms which are, or have become, resistant to penicillin. This is especially true in the treatment of staphylococcal infections of all types. Erythromycin is well tolerated by individuals who may be allergic to penicillin.

Erythromycin is readily absorbed and diffuses readily into most body tissues.

There is no cross-resistance between erythromycin and oxytetracycline, aureomycin, chloramphenicol or streptomycin, but there is cross-resistance between erythromycin and carbomycin.

Erythromycin has been found effective in the treatment of staphylococcal, streptococcal, and pneumococcal infections. It is also effective in the treatment of infections with corynebacteria.

Erythromycin inhibits the growth of the clostridia, *Haemophilus pertussis, Neisseria gonorrhoeae* and *Actinomyces israeli*.

To date, no serious toxic reactions have occurred following the use of therapeutically effective doses of erythromycin.

The widespread indiscriminate use of the antibiotic may invite the development of resistance and thereby seriously jeopardize its value in the treatment of certain types of infections.

For the average adult the oral dose of erythromycin is 300 mg. (occasionally 400 mg.) every six hours. For the average child the usual dose is 200 mg. every six hours. For infants and young children 100 mg. every six hours is recommended. This represents a daily dose of approximately 20 to 25 mg. per kilogram of body weight.

CITROVORUM FACTOR IN NUTRITIONAL MACROCYTIC ANAEMIA

NARAYANA AND OTHERS (*Indian J. M. Sc.*, **8**: 131, 1954) write that the isolation of folic acid, vitamin B_{12} and citrovorum factor in purified form and the demonstration of their effects in macrocytic anaemias have, in recent years, stimulated much interest in the pathogenesis of megaloblastic anaemias.

The effect of citrovorum factor on the blood picture of five cases of nutritional macrocytic anaemia was studied. Twenty-four milligrammes of a synthetic form of the factor (Leucovorin) was given in a single dose intramuscularly to each case. There was a prompt clinical and haematological improvement during the first two weeks following the injection.

Two patients suffering from nutritional macrocytic anaemia were treated with vitamin B_{12} which was also given in a single dose of 120 microgrammes intramuscularly to each patient. The response during the first two weeks was similar to that observed in the patients treated with CF.

With the dosages used in this study, vitamin B_{12} continued to improve the blood picture after two weeks of its administration while citrovorum factor failed to do so.

ENCEPHALITIS

KOTHARE (*Indian M. Gaz.*, **88**: 583, 1953) in reporting on eleven cases of encephalitis observes that in two cases the histological changes were highly suggestive of early encephalitis, in three the histology was typical of encephalitis, in one the diagnosis of post-vaccinal encephalitis could be made, in another acute polio-encephalomyelitis could be diagnosed and in four others extensive haemorrhages in the basal ganglia, midbrain and the pons were detected. The histological changes in these cases were characterised by haemorrhages, extensive neuronal damage, fibrinoid degeneration and arteriolar necrosis.

In three out of these four cases unsuccessful attempts to isolate a virus were made.

COMBINED CORTICOTROPHIN THERAPY AND CHEMOTHERAPY IN PULMONARY TUBERCULOSIS

HOUGHTON (*Lancet*, **1**: 595, 1954) in reporting on the combined corticotrophin therapy and chemotherapy in pulmonary tuberculosis with special reference to hypersensitive reaction writes:

21 patients with active pulmonary tuberculosis were given corticotrophin in combination with streptomycin and P.A.S. 8 of them were known to have an acquired hypersensitivity to one or both these drugs. The corticotrophin suppressed all the reactions during a standard course of chemotherapy. On withdrawal of the corticotrophin 6 of the 8 patients had lost their hypersensitivity.

5 of the 21 patients had gastro-intestinal intolerance to P.A.S., and this was suppressed by a very small maintenance dosage of corticotrophin.

5 patients were given corticotrophin in combination with streptomycin and P.A.S. in the absence of hypersensitivity.

3 patients who developed alarming hypersensitive reactions derived immediate benefit from corticotrophin.

No adverse clinical or radiographic effects were seen either during corticotrophin therapy or after its withdrawal for periods of up to two years.

On combined corticotrophin therapy and chemotherapy severely ill patients improved very much and the progress was maintained after the withdrawal of corticotrophin. Clinical and radiographic improvement was noted in patients who had not previously responded well to streptomycin and P.A.S. alone.

PYLORIC MUCOSA AND VITAMIN B_{12} IN PERNICIOUS ANAEMIA

MEULLENGRACHT (*Brit. M. J.*, **1**: 838, 1954) writes that it has been shown that even very small doses of dried pyloric mucosa from the pig's stomach given alone exert a definite but, in comparison with Bethell and Goldhamer's and Schiodt's standards, slight anti-anaemic effect.

It has also been demonstrated that the same very small amounts of pyloric mucosa, when combined with vitamin B_{12} in quantities which in themselves are inactive when given orally, exert a strong anti-anaemic effect which is practically the same as the standards referred to.

A commercial preparation, cycoplex mco, in daily dosage of 0·15 g. of dried pyloric mucosa and 15μg. of vitamin B_{12} exerts a strong anti-anaemic effect which corresponds to the standards cited. In the routine treatment of pernicious

anaemia patients, in order to be well on the safe side, a dosage is recommended which corresponds to 0·3 g. of dried pyloric mucosa and 30 μg. of vitamin B_{12} for the initial doses. The maintenance dose has yet to be fixed.

INSUFFLATION OF VITAMIN B_{12} IN PERNICIOUS ANAEMIA

ISRAELES AND OTHERS (*Lancet*, 1: 341, 1954) write that vitamin B_{12} is therapeutically effective when administered by insufflation in the form of snuff in patients with pernicious anaemia. The authors began by giving more than the usual intramuscular dose to allow for loss during insufflation and loss by swallowing but it proved only necessary to give the same order of dose that is effective by the intramuscular route. They gave 100 μg. twice daily for 4 days to one case and 300 μg. daily for 3 days to another case with good reticulocyte response and satisfactory increases in haemoglobin and red cells. For maintenance 100 μg. twice weekly was given but this may well be cut down to 100 μg. once a week. Thus this treatment is relatively inexpensive and is a useful alternative to intramuscular injections for suitable patients.

LIMITATION IN THE USE OF ROENTGEN EXAMINATION OF THE GASTROINTESTINAL TRACT

SWENSON AND JEFFREY (*J.A.M.A.*, 153: 1422, 1953) write that just as it is true that pathological change cannot be correctly interpreted when normal variants are not known, it is also true that any diagnostic study reaches its full value only when its limitations are well known and carefully considered.

There are several instances in which a properly conducted and interpreted roentgen examination of the gastrointestinal tract may yield results that are conflicting or fallacious. The first instance is a completely normal-appearing study when actually abnormality exists. A second instance is the finding of a structural or functional change, but failure to correctly interpret it. A third instance occurs in the study of specific areas of the gastrointestinal tract where it is difficult, at times, to demonstrate abnormalities even when they are known to be present.

The following are some of the limitations encountered and they are discussed under different heads:

Oesophagus—The first is the possibility of missing rather small lesions in the mucosal surface by not having several films with different degrees of filling. Varicosities, unless they are very far advanced, may often escape detection, because peristalsis may "milk" them out; or they may be collapsed from recent haemorrhage. Another rather annoying limitation of the examination of the oesophagus is the difficulty of detecting small superficial ulceration associated with a diaphragmatic hernia or acute peptic ulceration.

Stomach—The greatest difficulty is at the upper end where palpation is not readily carried out. It is easy to miss small lesions. This has been called the radiological "blind spot." Intramural lesions often give trouble unless careful fluoroscopy or a large series of films will show an apparent inflexibility of the stomach wall.

One of the greatest problems is distinguishing between a simple ulcer and an ulcer based on cancer or associated with a cancer.

The radiologist is usually correct in his interpretation when he finds that the lesion appears radiographically benign. An ulcer that is associated with cancer rarely decreases in size or disappears with a dietary regimen. The portion of stomach wall in which a malignant ulcer is present does not return to its usual normal flexibility, whereas almost always a complete restitution to normal occurs in a case of simple ulcer.

Small intestine and colon—In the small intestine the intramural lesion that may produce very little effect on the mucosa of the wall is obviously very difficult to demonstrate. The obstruction appears relatively late, and the barium moves through rather rapidly so that, unless careful fluoroscopy is carried out, lesions of this sort are easily missed. The nonspecific finding of a swollen irregular mucosal pattern with segmentation and sometimes widening of the lumen can be caused by either local intramural changes or mesenteric involvement, in which case either the intramural nervous mechanism or the lymph-vascular and blood supply is affected.

In the colon the size of the lesion is the only limitation (if careful preparation is carried out), since the examination can be better controlled than elsewhere in the gastrointestinal tract.

SURGICAL MANAGEMENT OF GASTRODUODENAL HAEMORRHAGE

FERGUSON (*Lancet*, 1: 228, 1954) from an analysis of 17 cases of gastroduodenal haemorrhage treated surgically observes:

Blood-transfusion is necessary for most patients whose Hb is less than 70 per cent. Surgery has an important place in the management of the elderly patient.

It is suggested that patients should be grouped for treatment as follows:

(1) Aged less than 45: medical treatment.

(2) Aged 45 or more:

(a) Aged 45-60: selective surgical intervention.

(b) Previous haematemesis: immediate operation.

(c) More than 60 (particularly if more than 70 or with coronary disease): immediate operation.

(d) More than 60 without history of peptic ulceration: initial medical treatment, and early surgery if bleeding recurs or continues.

VESICOVAGINAL FISTULAE

MOIR (*Lancet*, 1: 67, 1954) from analysis of 100 consetive cases of vesicovaginal fistula observes:

In most of them (75 per cent) there had been one or more previous attempts at surgical repair, and in many there were features that had caused the fistula to be regarded as intractable. The series does not include cases in which active carcinomatous growth was present.

In all the cases the fistula was closed. When the bladder alone was involved, the results were eminently satisfactory. When the urethra had to be completely reconstructed, the results, although occasionally excellent, were sometimes marred by continuing stress incontinence of urine.

Operation was by the vaginal route in every case of vesicovaginal and urethrovaginal fistula.

Many cases presented features of unusual clinical or anatomical interest; multiple vesicovaginal fistulae; ureterovaginal fistulae complicating vesicovaginal fistulae; vesicocervical fistulae; vesicocolic fistula complicating vesicovaginal fistula; vesical calculus complicating vesicovaginal fistula; rectovaginal fistulae complicating vesicovaginal fistula; and inver-

sion of the bladder through the fistula, simulating a prolapse of the uterus.

Vesicovaginal fistulae caused by necrosis following radium treatment are especially difficult to treat, but a satisfactory result is sometimes possible.

Long duration of a fistula is not a contra-indication to surgical repair.

The size of the fistula gives no certain indication of the case or otherwise of repair. Some large fistulae are easily closed; some small fistulae can present great difficulty in closure.

A plea is made for the careful and adequate treatment of vesicovaginal fistulae at the time of their occurrence.

TREATMENT OF PREMENSTRUAL TENSION

GREENHILL (*International Record of Medicine and General Practice Clinics*, **166**: 502, 1954, Ref. *Practitioner*, **172**: 331, 1954) on the grounds that premenstrual tension is due to water retention in the tissues, recommends its treatment with ammonium chloride—3 g. daily, in three divided doses, starting twelve to fourteen days before the expected menstrual period. In order to restrict sodium intake, patients are also advised to give up using table salt during this time. With this treatment he has obtained satisfactory results in 90 per cent of a series of 300 patients. The symptoms of which these patients were relieved included headache, emotional instability, irritability, abdominal distension and nausea. Most of the patients stated that they had an increased sense of well-being in addition to freedom from distress, while taking the ammonium chloride. The observation was made that 'many of the patients on ammonium chloride therapy are unaware of an impending menstrual period, which they could formerly predict a number of days in advance.' It is added that 'the administration of ammonium chloride is of little use in alleviating migraine unrelated to the menstrual cycle, dysmenorrhoea, or pain in the breasts.

NASOPHARYNGEAL IRRADIATION IN DEFECTIVE HEARING

DORAISWAMI AND SUBRAMANIAM (*Indian J. Radiol.*, **8**: 38, 1954) write:

Nasopharyngeal irradiation with either radium or deep x-rays is useful in cases of conductive deafness, when the cause of deafness is suspected to be due to hyperplasia of the lymphoid tissue situated near the opening of the eustachian tube. Out of a total of 150 cases observed, 100 were boys and 50 girls. So this condition seems to be prevalent much more in boys than in girls in the proportion of 2:1. The age incidence of these patients is commonly between 10-30 years, but the condition is more among children than adults.

The authors' methods of irradiation is by the use of deep x-ray exposure to the nasopharynx from the outside. This method seems to have certain advantages over the radium application, viz., (1) easier availability since radium in the applicator cannot be used for a variety of diseases; (2) insertion of the radium applicator is often painful and difficult especially in children and in cases of deviated nasal septum; (3) there has been report of damage and destruction of the cartilaginous eustachian tube due to the radium application, whereas it has been absent with deep x-ray exposure.

Deep X-ray Technique—The technique was evolved after a series of varying dosage factors. The following factors were found suitable and practically with no untoward reactions.

200 K. V., ½ cu. plus 1 Al. filtration, 50 cm. F.S.D.; 10 cm. circular cone to cover the entire nasopharynx.

150 r to either side, repeated at intervals of 3 or 4 weeks, thrice or 4 times.

Radium Technique and Dosage—The monel metal container that is used has an handle of 13 cm. length and contains 50 mg. of radium.

Active length of model metal container is 1·5 cm. and has a wall thickness of 0·3 mm. Cross-section of the container is 23 mm.

The authors use the same technique as Dr. Crowe. This consists in the use of 50 mg. of radium in a model metal applicator, which is inserted into the nasopharynx through the nostril and kept there for a period of 12 minutes on each side. This procedure is repeated 3 or 4 times at intervals of 3 weeks.

Results—Out of 50 cases that were subjected to deep x-ray therapy, 32 cases have shown definite improvement and also maintained a steady improvement for quite a long period and that is 64 per cent success. An equal number of cases were treated with radium and results were practically the same. There was difficulty in applying radium to many cases due to reasons already stated.

This study is based on observations on a number of cases, many followed up for 5 years or more. The hearing has improved in a large percentage and has maintained a steady improvement.

These small doses, at such long intervals between the exposures cannot do any injury to the centres of ossification, cartilage, nerve or mucous membrane but according to observations are quite enough to resolve excessive lymphoid tissues.

DIARRHOEA IN CHILDREN IN CEYLON

DESILVA (*Indian J. Mental Health*, **3**: 103, 1954) gives in the following lines the summary of his observation on the problem of diarrhoea in children in Ceylon:

Salmonellosis was the commonest single finding in diarrhoea in the Children's Hospital, Colombo, during a period of three years.

Of the cases that developed a second infection in the ward with a different type of salmonella, the majority showed a fresh attack of diarrhoea, or other adverse signs and symptoms, proving its pathogenicity.

S. adelaide and S. virchow were the commonest strains isolated and accounted for 80 per cent of the cases between them.

The salmonella infections were mainly intramural in origin.

Most strains of *S. virchow* were insensitive to all antibiotics except aureomycin. In a fair proportion of strains *S. adelaide* was however sensitive to most of the wide-spectrum, newer antibiotics except terramycin and erythromycin.

Among children shigellosis was much less common than salmonellosis.

While 1951 did not show a single case of shigellosis at the Children's Hospital, 1952-1953 showed a considerable number of such cases.

The fatality rates of shigellosis and salmonellosis were the same.

There was a fair number of mixed infections—both of different types of salmonellae and of those with shigellae.

E. coli 0·111: B4 and 0·55: B5 were not factors of importance in the aetiology of infantile or neonatal diarrhoeas in Colombo from 1951 to 1953.

SALT INTOXICATION?

The risks of administering excessive saline parenterally are well appreciated; but the possibility of inducing a harmful excess of salt in the body by feeding salt has been generally discounted, at any rate in people with normal kidneys which are not under the influence of salt-retaining hormones. It has been known for some time, however, that a high-salt intake potentiates the hypertension induced by deoxycortone acetate (Selye and Hall—*Arch. Path.*, **36**: 19, 1943), and conversely that a rigorous low-salt diet can substantially reduce blood-pressure in many hypertensive patients (Kempner—*N. Carolina M. J.*, **6**: 61, 1945). There is therefore a distinct possibility that long-continued excessive salt intake may be deleterious, even though it does not lead to obvious oedema and plethora. The effects of varying the salt intake in an otherwise constant diet have been studied in rats by Meneely *et al* (*Ann. Int. Med.*, **39**: 991, 1953).

The experimental diets were fed to groups of rats for up to nine months. The basic diet was practically salt-free, and salt was added to it in varying amount to give six diets with a salt content ranging from 0·15 per cent of the total diet (the proportion commonly used in nutrition experiments) to as much as 9·8 per cent. The most dramatic findings were in the three groups on diets with 7·0 per cent, 8·4 per cent, and 9·8 per cent salt. No person is likely to take a diet with such proportions of salt, for even a 7 per cent intake would correspond to 50 g. or more of salt per day. Of 90 rats in these three groups, 18 per cent developed oedema, hypertension, anaemia, lipaemia, hypoproteinaemia, and azotaemia; and most of these animals died. The animals eating the high-salt diets also passed large volumes of urine, independently of renal failure. This is not perhaps a surprising finding; nor indeed is it a novel one, for Meneely *et al* (*loc. cit.*) cite a corresponding observation in 1814 on cattle given salted hay. Perhaps the finding most likely to be related to clinical problems is the steady increase in systolic blood-pressure as the salt content of the diet increased; the increase was already present at a level of salt intake corresponding to 12 g. per day in man. The consistency of the blood-pressure increase is perhaps more impressive than its extent, for the whole range from low-salt to 10 per cent salt diet is only about 30 mm. Hg. The slightness of the difference in blood-pressure between the low-salt and normal-salt groups is at variance with clinical experience, at least in hypertensives. The rats exposed to high-salt diets showed widespread arteriolar and glomerular changes in the kidneys, "resembling malignant hypertension."

Meneely *et al* urge caution in interpreting these results; and the conjunction of massive renal oedema with arteriolar necrosis should perhaps discourage any facile transfer of ideas to kidney disease in man. Salt restriction is generally thought to have little influence on essential hypertension until the level of dietary salt has fallen very low; but it is just possible that further investigation in man might show that diets of moderate and of high salt content are associated with differences in blood-pressure. Feeding of extra salt to hypertensive patients would be unjustified, but it might be worth comparing blood-pressure levels with gross variations in twenty-four-hour chloride output. Those interested in the geographical distribution of diseases could probe further the alleged low incidence of hypertension in the Asian land-mass, where salt is at a premium; while the medical historians might have some notion of how our forebears' winter diet of pickled beef compared with the alleged stresses of modern life.—*Lancet, Annot.*, **1**: 146, 1954.

CARCINOMA OF THE FEMALE BREAST

WILLIAMS AND OTHERS (*Brit. M. J.*, **2**: 787, 1953) give in the following lines the summary of their observations:

The purpose of the paper is to present an analysis of the results obtained in 1,044 cases of carcinoma of the female breast first seen at St. Bartholomew's Hospital during 1930-9.

Follow-up of all but 30 untraced patients was complete until May, 1951, enabling 10-year survival rates to be calculated for the whole series and 15-year rates for cases registered in 1930-5.

The distribution by clinical stages was as follows: I, 32·5 per cent; II, 28·9 per cent; III, 27·4 per cent; IV, 10·2 per cent; unstaged, 1·1 per cent. Distribution by age and site of tumour was similar to that given in other published series.

Differences in clinical staging are not explicable only in terms of delay in seeking advice. Of cases with more than two years' history 31 per cent were still in stage I, whilst 19 per cent of those with a history of one month or less were in stages III and IV.

Pathological investigation of cases with axillary dissection revealed that the clinical assessment of the glands was wrong in 29 per cent of stage I cases and 23 per cent of stage II cases. There was no clear association between length of history and gland involvement.

The various methods of treatment are discussed. Simple surgery was undertaken in 229 cases, more than half of which were treated by simple excision of the tumour. Radical mastectomy was done in 338 cases, and the modified radical operation in 167. Radium treatment without surgery was used in 149 cases, and x-rays alone in 114. Forty-seven cases were not treated. Of the cases treated surgically, about two-thirds were also given irradiation. This type of treatment became more frequent towards the end of the period, and at the same time x-rays tended to replace radium, particularly in combination with simple surgery.

Five and ten-year survival rates, adjusted for variations in age distribution, are calculated for different clinical stages and treatment groups. The adjusted rates for all treated cases in stage I were as follows: five-year, 72 per cent; ten-year 51 per cent. The corresponding figures for stage II were: 39 per cent and 26 per cent. The rates for the individual treatment groups showed no appreciable departure from these figures despite the fact that simple surgery consisted merely of local excision in more than half the cases; nor did the addition of irradiation affect the rates, although it is possible that selection of cases may have concealed some of the benefits of radiotherapy.

Attention is drawn to the lower survival rates in the cases assessed clinically to be in stage II but with axillary glands pathologically free, compared with stage I cases with glands involved.

The mortality of radical mastectomy was 1·2 per cent. Oedema of the arm occurred after radical surgery in 14 per cent of cases, compared with 5 per cent after simple surgery, and was almost twice as frequent when the radical wound gave rise to complications as in those with primary healing.

There seemed to be fewer local recurrences following radical surgery than other types of surgery, but the addition of radiotherapy appeared to make no difference in this respect.

It was concluded from a general discussion that where efficient radiotherapy is available radical mastectomy should be abandoned in favour of conservative surgery.

ANTIBIOTICS IN WHOOPING-COUGH

Whooping-cough remains a serious disease, especially in very young children, and unfortunately antibiotics offer no dramatic benefits. *Haemophilus pertussis* is highly susceptible *in vitro* to the action of the newer antibiotics, yet their efficacy in the treatment of the disease is still uncertain. This is perhaps not surprising in view of the fact that, in the untreated disease, *H. pertussis* disappears early from the clinical picture, though symptoms persist and often increase for several weeks after it can no longer be detected. Perhaps *H. pertussis* induces an altered state of the tissues which is responsible for the symptoms, and once this state is induced the presence or absence of the organism is of little account. A drug whose only action is to inhibit *H. pertussis* could not be expected to alter the course of the disease unless it were applied before the tissue reaction had been induced. While this is no more than conjecture, something of the sort may explain the discrepancy between clinical and laboratory results.

A report (*Lancet*, **1**: 1109, 1953) published by the Whooping-Cough Sub-committee of the Antibiotic Clinical Trials Committee of the Medical Research Council analysed the results of treatment with chloramphenicol, aureomycin, and an inert control preparation in 294 patients. Children aged 0-11 months were given 1 g. daily in two doses, children aged 12-35 months 1·5 g. daily, and children aged 36-59 months 2 g. daily, in each case for seven days. The effect of the treatment was judged by the frequency and severity of the spasms and by the culturing of per-nasal swabs. The bacteriological evidence was clear: treated cases cleared more rapidly than controls. Clinical effects were much less striking, and it was mainly in cases treated within eight days of the onset of the earliest symptoms that any significant difference was found. The report emphasizes that these earliest symptoms are cough or coryza, not the development of a paroxysmal cough, which for this purpose must be regarded as appearing at a relatively late stage of the disease. It is also clear from the report that even in the early group, results of treatment were not dramatic: indeed, most of the children were still having typical spasms three weeks after the start of treatment. The drugs appeared to diminish the severity of the paroxysms to a greater degree than their number. But in cases treated later than eight days after the onset of symptoms the difference in number and severity of paroxysms between treated and control groups was very slight, though always in favour of the treated group. As the report states, if attention had been directed to a comparison between the whole of the treated and of the control groups, it would have been concluded that chemotherapy failed to produce a clear-cut clinical cure.

Gray (*Lancet*, **1**: 1257, 1953) commenting on the report, criticized a dosage scheme based on age rather than tissue mass. He worked out the equivalent doses per kg. body weight: these range from 50 mg. to 75 mg. per kg. It is quite possible that such doses are not high enough, but they are not unreasonably low. Gray then quoted some figures of chloramphenicol concentrations in post-mortem lung and brain tissues showing that concentrations of the drug vary from tissue to tissue, that vascular obstruction coincides with low concentration, and that in uninflamed human lung chloramphenicol is rapidly removed. These are points of considerable importance, suggesting that different dosage may be required at different stages of the disease, but whether they can be translated into a practical dosage scheme is another matter. In an earlier paper Gray (*Lancet*, **2**: 800, 1950) investigated the use of aureomycin and chloramphenicol in the treatment of whooping-cough: for aureomycin the dosage was 50 mg. per kg. per day in four doses, for chloramphenicol 100 mg. per kg. per day in one dose, in both cases for a total of five days. He found that both drugs reduced the number of coughs, but that chloramphenicol also lessened the whooping and vomiting and loosened the cough. His results showed no dramatic change in the course of the disease: children were still having paroxysms three weeks after the onset of the disease, but the number of paroxysms was less than in the controls. He suggested a higher dosage scheme.

Other workers have had similar experiences. La Boccetta (*Am. J. Dis. Child.*, **84**: 184, 1952), using aureomycin in a dosage of 50 mg. per kg. body weight for ten days, concluded that, except in cases treated in the first week of the disease, there was no marked apparent effect from the use of the drug. Lassen (*Lancet*, **1**: 763, 1951) treated 93 cases with chloramphenicol, given as rectal suppositories for three to five days, and claimed that the frequency of the paroxysms fell sharply. No untreated controls are reported for comparison, and patients were still having paroxysms at the end of the period of observation, though fewer in number. Hazen (*J. Pediat.*, **39**: 1, 1951) and Booher (*Ibid*, **38**: 411, 1951) used terramycin as well as the other two drugs, and it appears to have a similar degree of efficacy. Bogdan (*Lancet*, **1**: 764, 1951) used chloramphenicol to treat contacts, and his results are striking: in 10 out of 13 cases the disease was arrested in the pre-paroxysmal stage. The treated contacts must be isolated from infectious cases to avoid reinfection.

It is clear that no drug has yet been discovered which will rapidly control an attack of whooping-cough. Aureomycin, chloramphenicol, and terramycin probably all have some effect if given in the earliest stages, but the effect is far from dramatic. When given later in the disease they have very little effect. These drugs have toxic effects—most notably chloramphenicol—and it is inadvisable to prescribe them in every case. The minimal dosage is 50 mg. per kg. body weight per day, and 75 or 100 mg. per kg. may be better given in three or four doses per 24 hours for seven days. Because babies under 1 year suffer most severely from the disease, it is justifiable to treat all patients of that age. All cases diagnosed within a week of the first symptom—not the first spasm—might also be treated. Even in these cases dramatic results should not be expected. Probably the most rational use of the drugs is in the treatment of contacts before they develop the typical symptoms of the disease.—Ed. *Brit. M. J.*, **2**: 769, 1953.

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CURRENT TOPIC

MEDICAL PROFESSION TO-DAY*

K. C. O.

HEALTH INSURANCE WON'T SOLVE DIFFICULTIES

The articles by F. G. published in the "Indian Express" have stimulated considerable interest in the problems discussed. The diversity of views expressed however is an index alike of the complexity of the problem and the impossibility of finding remedies acceptable to all.

It is tragic that while the country has only a third of the number of doctors required to attain the modest target of one doctor for 2,000 people, and much of the rural area, representing about 80 per cent of the population remains outside the pale of modern medicine, the majority of doctors should remain underemployed and try to earn a living by unhealthy competition or by "turning tradesmen."

The remedies suggested appear to bristle with difficulties. As one who has for a whole lifetime pressed for better salaries for doctors in Government service, I shall be very happy if the I.A.S. scale of salary be granted to them. But there is a growing feeling that the I.A.S. scale, low though it is, is above the financial resources of many States. Also it has to be remembered that the I.A.S. is a Central Service recruited on the basis of a stiff all-India competition. The Medicos and the Engineers have Central cadres comparable to the I.A.S. The heavy financial burdens apart, no State Government can introduce such a radical reform in one of its departments only. Neither can one group of officers, in any department, be alone treated favourably ignoring the different grades of subordinate officers who are equal sufferers.

The Employees Insurance Corporation is undoubtedly a memorable landmark in the country's social evolution. It will, however, be premature to expect early relief for the rural population or for the underemployed doctor, from this infant reform. Even the most socially advanced countries present such variations of pattern in health insurance, that there is no dependable model for us to follow. The panel system of the United Kingdom is not what obtains in Australia, Canada or New Zealand. Naturally, the Employees Insurance Corporation has not committed itself to a uniform policy for the whole country. While Kanpur has full-time Insurance Medical Officers, the Punjab is trying the panel system. The Insurance Medical Officers in Kanpur belong to the State Health Service and are posted for insurance work with an extra allowance of Rs. 50 to 100—depending on years of service—to compensate for loss of private practice. The report is that they are already dissatisfied. In the Punjab, the capitation fee was considered too low and so the Punjab Branch of the Indian Medical Association did not accept it.

Although the Insurance Corporation was inaugurated in 1948, the Insurance Scheme came into operation (in three centres) only in 1952, and in 1954, the terms and conditions for its further limited extension are still under negotiation between the Corporation and the Indian Medical Association. Because of the difficulties inherent in this reform and its consequent slow and halting progress, it is to be doubted if its extension to include agricultural labour will be possible in the near future.

And if any State takes courage in both hands to bless agricultural labour with health insurance, there is little assurance that the scale of remuneration will be the same as proposed now. Also for financial reasons, if not for anything else, the graduates and licentiates of the Indigenous Systems might be selected for this work. As stated by the Health Minister of Madras, in the current session of the Madras Assembly, 234 out of the 411 rural dispensaries in that State are now under this class of practitioners. It is worth remembering that the Insurance Corporation had to toe the line and recognise the eligibility of qualified practitioners of homoeopathy and the indigenous systems for insurance work.

State Governments, financially hard pressed, are following the line of least resistance and trying to capitalise the sentimental predilection of the masses for the indigenous systems to dole out a low standard of service in modern medicine, sugar-coated as indigenous medicine.

This is the ominous rock which threatens to split not only the laudable suggestions of F. G., i.e. enhancement of scales of pay and extension of health insurance to the rural population, but even the unchequered progress of scientific medicine in the country.

For a satisfactory solution of the difficulties which confront the medical profession and the country this grave danger ahead—the attempt to perpetuate at public cost and with official recognition a number of separate systems of medicine with varying standards and conflicting ideologies—deserves immediate attention. The resolution passed at the last meeting of the Central Council of Health, held in Rajkot to start five-year degree courses in Ayurveda, Unani and Homoeopathy, should therefore be viewed with the utmost concern. The award of degrees and diplomas by institutions maintained or assisted by the State also implies the recognition of the eligibility of the successful candidates for employment in the service of the State.

Be it admitted at once, that inspite of its growth of over 150 years, modern medical practice remains qualitatively and quantitatively insufficient to meet the gigantic requirements of this country. Many a doctor is still being accused of the mercenary outlook and superiority complex. The country continues to import the vast bulk of drugs and instruments. The villages, the backbone of the nation, are being served chiefly by the Hakim and the Vaid. No attempts have been made to prepare an Indian Pharmacopoeia incorporating whatever might be useful in the indigenous systems and so these continue to be an enchanting mystery even to the educated leaders of the public.

It is therefore not surprising that popular Governments eager to extend rural medical service have accepted the indigenous systems (and some are flirting with homoeopathy) without reckoning the ultimate cost.

Promotion of positive health based on scientific prevention of diseases, is now admitted to be the fundamental function of medicine. Cure of disease itself has outgrown beyond all recognition the old empirical process of medication, with a number of highly specialised and scientifically assessable branches for diagnosis and treatment. Modern medicine alone fulfils these requirements. Therefore, no civilised country now spends public funds on medical education which falls short of the accepted minimum standard in scientific medicine.

What is now called scientific medicine was also an 'art,' not long ago. It was its slow and laborious passage on the anvil of physics, chemistry and biology that has led to its progressive transformation from an "art" to a "science."

*Reproduced from the *Indian Express*, April 30 and May 1, 1954.

The protagonists of the "art" of healing should know that "faith healers" are the real masters in this field; but they might not be aware that the diseases successfully treated by the "art" of healing' are essentially psychoneurotic in character.

To concede to every citizen "the right to seek medical relief as he chooses" will be ignoring the State's responsibility for the health of the people on which is based the wide network of national and international public health regulations. It will also be impossible to admit that "if a patient goes to a quack it is his own funeral,' without a radical revision of the present-day conception of suicide and homicide.

An amalgam of scientific medicine and indigenous medicine may prove more damaging than naked quackery, because the former will have the seal of official recognition. Unfortunately this is what is being done in the country, in the schools of indigenous medicine, and what is proposed to be extended by instituting degree and diploma courses, as resolved by the Central Council of Health, at Rajkot.

In all existing institutions of this kind more and more of modern medicine and less and less of indigenous medicine are being taught as is frankly admitted by the Director of Information, Madras.

The situation is amazing. The Indian Medical Council, the supreme authority for controlling education in modern medicine, after years of persistent efforts, has succeeded in getting the M.B.B.S. Degree accepted as the minimum standard for registration. Barring a couple of exceptions, which are in the process of liquidation, the medical schools which offered the licentiate course, have been upgraded as colleges or abolished. Medical Councils have been constituted in the States for granting registration and for supervising the professional conduct of the registered practitioners.

It is therefore amazing that instruction in modern medicine can be given in Government schools and colleges without the approval of the Indian Medical Council or the State Medical Councils. It is more amazing that registration under the Councils or Boards of Indigenous Medicine will suffice for the practice of modern medicine.

The progress of generations is threatened with irredeemable setback. The danger of 'debacle' lies more in this direction than the proposed training of auxiliary health personnel, which in any case being subordinate to the fully constituted modern health service can be stopped as soon as the pressing necessity is over.

The competition from 'amateur doctors . . . . . genuine or self-styled Vaids and Hakims" can be eliminated without heartburn to any one. The new T. C. Medical Practitioners Act has such a provision. All persons engaged in bonafide medical practice on the day on which the Act came into operation will be allowed to continue as listed practitioners. This was what was done in the United Kingdom when medical registration was introduced. No person can be statutorily debarred from practising the profession from which he was legitimately earning his living. While tolerating the survival of established quacks, the future is safeguarded by stipulating that henceforth only persons with recognised qualification will be entitled to register and to practise. Legislation of this kind which is among the major recommendations of the Bhore Committee, if introduced in all the States, will within a reasonable time, protect the public as well as the doctors from quacks.

New Outlook Needed with Bias for Rural Service

The growing number of licentiates and graduates from the so-called schools of indigenous medicine who claim to embody "the synthesis of the best in the Indian and foreign systems" presents a more formidable threat of increasing magnitude. The solution of this problem is admittedly difficult for reasons briefly recounted already, but its continuance is fraught with such catastrophic consequences that it merits the highest priority of consideration by the leaders of the public and the medical profession. The only reasonable solution will be to separate the grain from the chaff in the indigenous systems and use the grain and discard the chaff.

A time limit should be prescribed—15 or 20 years—after which public funds should not be spent on institutions teaching or practising the indigenous systems of medicine either alone or in sub-standard combination with modern medicine This is what New China has done with reference to their indigenous systems which have as hoary a past as ours.

During this period a nationwide intensive research should be undertaken to sieve out whatever might be useful in the indigenous systems. In the hospitals attached to the schools of indigenous medicine and in other State-aided hospitals specialists in these systems should carry out treatment in selected cases. Experts in modern medicine should be allowed to establish their own diagnosis in these cases, watch the progress and compare it with their own results obtained in similar cases. A committee consisting of non-medical scientists, professors of chemistry, biology, physics and statistics, may be helpful in impartially assessing the results.

An investigation like this, under the guidance of a central committee, carried out in all the States spending public funds on indigenous systems will, in 15 or 20 years, reveal what is worth preserving in them. That can be incorporated in an Indian Pharmacopoeia and included in the syllabus for the M.B.B.S. Course.

When this is done there can be no valid reason for the maintenance of separate institutions for teaching or practising these systems. Post-graduate research as well as post-graduate courses in the ancient systems of medicine can be instituted in the Medical Colleges to make it doubly sure that whatever may be useful is preserved and developed for the benefit of mankind. Post-graduate courses can be instituted in other systems like Homoeopathy, Hydropathy, etc., when there is demand. There can be no objection to any supplementary post-graduate course. But to substitute part of the M.B.B.S. syllabus at the undergraduate level, with texts in other systems, will result in monstrous hybridization.

If the above suggestions are accepted, the interim period of 15 to 20 years requires careful handling so that at the expiry of that period there are no complicated legacies left over. The immediate abolition of the indigenous schools, advocated by Dr. Krishnaswamy, will be generally endorsed by the medical profession. But for two reasons this is impossible. One is the mass psychology which, worked up to a frenzy by about 5 lakhs of followers of these systems, cannot be ignored by any popular Government. The other is the urgent extension of cheap rural medical relief.

So the schools and colleges teaching indigenous medicine, either alone or with varying doses of modern medicine, have to be accepted as an inescapable feature of this passing phase and ways and means sought for making the best use of them.

Modern medicine of varying order is now being taught in all schools of indigenous medicine. Some definite and acceptable standards in modern medicine should be made compulsory and it should be the duty of the proper authority—the State Medical Council—to prescribe and enforce that standard. If after training they are to work as independent practitioners of modern medicine they should be registered under the Medical Council for modern medicine and the standard should not be lower than that of the licentiates. It may be possible for the more enterprising among them to take the condensed course for the M.B.B.S. just as licentiates have been doing for some time, in case the minimum entrance qualification is fixed as a creditable pass in the I.Sc.

A lower grade of training may be permissible for auxiliary health personnel on the definite understanding that they shall, at no time, have the status of medical practitioners but shall function on the lines on which Dressers of Malaya and Apothecaries of Ceylon work—under the direct supervision of registered medical practitioners. Their training also should conform to standards prescribed by the competent authority in modern medicine. If instruction in modern medicine offered by the schools for indigenous systems be thus regulated and controlled, it will be possible to fit the successful candidate in any co-ordinated scheme of Health Services.

The abolition of such lower grade of training will depend upon the speed with which fully qualified doctors become available for the country's needs, especially for rural medical service. This in turn depends upon several factors of which number is only one. The Minister of Health, Madras, admitted a few days ago, in the course of a debate in the Madras Assembly, that the village vaids, who were specially trained to serve as auxiliary health personnel in the villages, were trying to get away to the urban centres. It is not, therefore, surprising that young doctors used to urban life prefer under-employment in cities to more remunerative rural work. So the conditions of a service should be made more attractive. A uniform scale of salary for the whole country may be impossible. But even States like Mysore and Travancore-Cochin ought to lose no time in fixing the basic pay of doctors at Rs. 200 rising to Rs. 500 by a time scale with a sufficient number of higher posts which the better qualified and the more efficient can aspire to reach before they retire.

The right of private practice granted to full-time medical officers is the excuse for the prevailing low salaries. This vicious system has, however, earned for many a Government hospital and dispensary, established for the free treatment of the poor the odium of being subsidised institutions for the private practice of the doctors in charge. And when the hospital is ill stocked as it frequently happens, the doctors are accused of having cornered all the useful drugs for their private practice. To state that "Private practice keeps the medical man on his toes" or to suggest that collections from paying patients should be divided among the employees (as Dr. Krishnaswamy has done) will only provoke the criticism, often heard, that the profession instead of existing for the people expects the people to exist for it.

Private practice by Government Medical Officers has been the chief obstacle to the healthy development of private medical service in many semi-urban and flourishing rural areas. The odds are heavily weighted against a young practitoner who has to compete with one or more medical officers with a free hospital or dispensary behind them.

This demoralising system, relic of an age when there were no private practitioners, should be stopped at once in the interests of every one concerned. The salaries of doctors, kept low in the hope of ample remuneration from private practice, should be suitably upgraded.

The abolition of quackery and the acceptance of the M.B.B.S. as the minimum registrable qualification implies a simultaneous obligation to provide the country with enough doctors—if not 1 for 2,000 as the Bhore Committee has recommended, at least 1 for 3,000 people. More Medical Colleges have been started in India during the last 10 years than during the previous 100 years. Nevertheless, if the average effective period of work of a doctor be reckoned as 30 years the number of new entrants into the profession, over and above the number necessary to replace those who go out of practice by retirement or death cannot be much above 1,000 per year. And to reach the target of 1 doctor for 3,000 people may take 60 years or more. So more Medical Colleges should be established to raise the output of doctors by at least 1,000 more per annum.

The question may be asked if, as F. G. has stated 76 per cent of the present number of 60,000 doctors are underemployed, what will happen when the total number is double in 20 or 25 years. And already some prominent members of the profession like Dr. Krishnaswamy think it "insane to create more doctors."

It has to be admitted that unless a miraculous transformation of the economic condition of the country occurs, the emoluments which the present day doctor gets may not be maintained when the number is doubled. The slogan of 'high investment and high return' will have to give way to 'low investment and medium return'.

The cost of medical education should be brought down substantially and poor deserving students should be given financial assistance to choose medicine as their career. It will be good to give applicants from rural areas some weightage in admissions to medical colleges. The rural student has often an unequal competition with his urban classmate and might fail to get sufficiently high marks for selection into medical colleges. Without sacrificing efficiency it may be possible to give him some weightage to compensate for the adverse conditions against which he has had to battle from the time of his entry into the primary school till his passing the I.Sc. There will be greater chance of his reconciling himself to a village life, after taking a degree in medicine, than will be the case with his urban classmates.

Increase in numbers by itself will be of little use. A new outlook—greater bias for rural service with more emphasis on prevention—should be created in the future generations of doctors. An experiment has been started in this direction in the new T. C. Medical College where a rural population 50,000 strong, in an area of 20 sq. miles adjacent to the College, has been selected as a model training centre for medical students. From the commencement of their undergraduate course the students are brought into close contact with the villagers and their problems. It is expected that after five or six years of such training the young medical graduate will find himself not only in greater harmony with village life but more competent to handle its problems than his predecessors.

The complaint is now universal that the hospitals and dispensaries are not adequately stocked. If owing to financial stringency existing institutions cannot be maintained

satisfactorily, the situation will be worse when more hospitals and dispensaries are opened.

The enormous financial drain involved in the import of medical supplies should be stopped as early as possible. The manufacture of chemicals and drugs including indigenous preparations of proved value, to make the country self-sufficient in this important field and to reduce the cost of medical relief, should have the highest priority in our developmental programme.

At the same time there should be an uncompromising crusade against the manufacturers of spurious drugs who are undermining confidence in Indian products.

The profession may be indignant at the proposal to make rural service a compulsory condition for entry into Government service. But indirectly this is being enforced in Mysore and Travancore-Cochin. Mysore takes a bond for 5 years' service under the Government from every medical student and Travancore-Cochin takes a bond for 3 years' service. In vindication of what might appear an outrage on fundamental rights, it is said that the State spends on the training of every medical graduate Rs. 10,000 to Rs. 15,000 and therefore it has a right to ask the young doctor to serve the poor tax-payer at least for a few years on conditions which it can afford. An impartial judge might well declare "much can be said on both sides."

The problems which face the medical profession are of vital concern both to the public and the profession. Unless tackled with goodwill and understanding these problems may lead to a disastrous setback in the country's march to the goal of a Welfare State. The medical profession, more especially the future generations of doctors can be expected to make all reasonable sacrifice for their country; but it is equally necessary that the leaders of the public should understand the problems in their correct perspective and appreciate the difficulties which beset the doctor.

NOTES AND NEWS

INDIAN COUNCIL OF MEDICAL RESEARCH

Applications are invited for grant-in-aid from the Indian Council of Medical Research to carry out medical research during 1955-56. All applications for grants should be forwarded, through proper channel, so as to reach the Secretary of the above Council not later than the 10th September, 1954.

One hundred and twenty copies of a note showing the lines of work to be undertaken should be forwarded with each proposal. To enable the Scientific Advisory Board and its Advisory Committee to assess accurately the value of the research work proposed, the note should give information on the following points:—

i. The exact problem to be investivated should be isolated and the question which the investigator proposes to study clearly defined.

ii. A resume of all the relevant literature available on the proposed research should be given.

iii. The lines of work and full details of the plan indicating the manner in which it is proposed to carry out the work should be described and the assistance that will be available from associate workers e.g., biochemists, radiologists, bacteriologists, pathologists, etc., should be mentioned along with the names, degrees and addresses of such workers.

iv. The worker should state his previous research experience on the problem proposed or on allied problems.

v. A worker should consult a competent statistician at his own centre in planning his work and indicate that this has been done in the note which he submits. This is particularly important in the planning of biological investigations and surveys.

vi. The problem submitted should be such as to be capable of solution within a reasonable time.

Proposals should include as accurate an estimate of expenditure as possible under various heads such as

i. Contingencies.
ii. Travelling allowance, if any
iii. Equipment and stores, and
iv. Animals and their upkeep.

Detailed information should be given as to the place where the research will be conducted, the laboratory facilities and equipment available.

The note on the proposal should have a front page on which should be given,

i. The title of the proposed research scheme.

ii. Full name with degrees, designation, etc., of the research worker.

iii. Place where the research will be carried out.

iv. The aim, object and scope of the work.

v. Previous work on the problem.

vi. The importance of the work—fundamental and academic or applied.

vii. The period required for the completion of the investigation.

viii. The exact requirements.

ix. A blank space of half a page, headed 'Recommendations by the Committee'.

It may please be noted that the grant is sanctioned by the Council on the explicit understanding that all the facilities required for conduct of the research scheme shall be available in the institution where research is conducted.

COLONEL AMIR CHAND TRUST FOR MEDICAL RESEARCH

Lieut.-Colonel Amir Chand, ex-Principal, Lady Hardinge Medical College, New Delhi, has made a munificent donation of Rs. 50,000/- to the Indian Council of Medical Research for the purpose of awarding prizes for the best published work in the field of medical sciences. The Governing Body of the Council has constituted a Trust called the 'Colonel Amir Chand Trust' for the administration and management of the Fund. Six prizes, of almost equal value, of which some may be in the form of medals, shall be awarded annually on an All-India basis for the best published research work in any subject pertaining to all fields of medical sciences in general including clinical research.

Three of the prizes will be known as, 'Basanti Devi Amir Chand Prize' and the other three, 'Shakuntla Amir Chand Prize'.

Out of the six prizes, two shall be awarded to graduates of not more than ten years standing. The competitors for the prizes may be medical or non-medical graduates.

In case of a joint publication the prize shall be divided between the joint workers in such proportion as the Selection Board may recommend.

In 1954, it has been decided to make a beginning by the award of two prizes of the approximate value of Rs. 300/- each for the best research papers in medical science published by workers during the academic year 1953.

The award of the prizes will be announced at the annual meetings of the Scientific Advisory Board and the Advisory Committees of the Indian Council of Medical Research to be held in Baroda in November/December, 1954.

The workers are required to submit 15 reprints of their papers published during 1953 and these should be sent to the Secretary, Indian Council of Medical Research, 'P' Block, Raisina Road, New Delhi, so as to reach him not later than the 15th October, 1954, along with a short biographical sketch and two copies of passport size photographs of the worker or workers concerned.

WORLD MEDICAL CONGRESS

A meeting of the International Committee of the World Congress of Doctors, Vienna, for the study of Present-Day Living Conditions has proposed that a Second World Conference should be held under the title "The Influence of Living and Working Conditions on Health" during September 1955.

CARDIOLOGICAL SOCIETY OF INDIA

The next annual Scientific Conference of the Cardiological Society of India will be held at Nagpur Medical College, Nagpur (M.P.) during the first half of the month of February 1955. The Jt. Hony. Secretary of the Society, 67, Dharamtala Street, Calcutta, may be contacted, for further particulars.

ALL-INDIA OBSTETRICS & GYNAECOLOGICAL CONGRESS

The 8th All-India Obstetrics & Gynaecological Congress will be held on 20th, 21st and 22nd of December, 1954 at Lady Hardinge Medical College, New Delhi. The following subjects would be discussed: 1. Abnormalities of the Third Stage of Labour, 2. Malignant Ovarian Neoplasms, 3. Statistical Survey (a) Newborn Infants regarding weight, length, circumference of head and chest, (b) Prolapse of the Uterus in relation to parity and age.

For further particulars please contact Hony. Secretary, Reception Committee, 8th All-India Obstetrics & Gynaecological Congress, New Delhi.

MADRAS MEDICAL COUNCIL

Dr. M. Ramanujam Naidu, L.M.P., (Madras) 1922, West Main Street, Padukottai, and Dr. Muthukumaraswami Pillai, L.M. & S. (Madras), 1919, 21 Second Line Beach, Nagapattinam, have been found guilty of infamous conduct in a professional respect and in exercise of the powers conferred on it by section 16 (2) of the Madras Medical Registration Act (IV of 1914) the Madras Medical Council directed that the name of Dr. Ramanujam Moorthy Naidu, L.M.P. (Madras) 1922 holder of Registration Certificate No. 2768, dated 14th May 1923 and the name of Dr. Muthukumaraswami Pillai Sambasivan L.M. & S. (Madras) 1919, holder of Registration Certificate No. 1924 be erased for one year and that their re-instatement will be subject to their producing certificates of good conduct from two registered medical practitioners.

BOMBAY MEDICAL COUNCIL

In a meeting of the Bombay Medial Council held on the 14th September 1953, Dr. L. V. Patankar, L.C.P.S.(BOM.) was found guilty of infamous conduct in a professional respect and the direction for removal of his name from the Medical Register was postponed for a period of six months subject to the condition that Dr. L. V. Patankar, L.C.P.S. (BOM.) should not grant certificates for the period of six months.

The Council in the same meeting decided that the qualification of D.C.H.(Eng.), be recognised for the purposes of registration as an additional qualification and that the same be added to Table (G) of the Bombay Medical Register.

ALL-INDIA SURGEONS CONFERENCE

The 16th All-India Surgeons Conference will be held in Hyderabad in the month of December 1954. Invitations have been extended to doctors all over India.

There will be Scientific Sessions, Film Shows, a Scientific Exhibition and Entertainments, etc. A Conference Souvenir is proposed to be published.

RAJKUMARI AMRIT KAUR ON STANDARDS OF PURITY AND POTENCY OF DRUGS

Inaugurating the Chloromycetin factory of Messrs. Parke, Davis and Co., Ltd., Bombay, on the 8th July, 1954, Rajkumari Amrit Kaur said *inter alia*, "I take this opportunity once again to emphasise the importance of maintaining adequate standards of purity and potency in the manufacture of drugs and medicines used in connection with prevention and treatment of disease. This country has suffered much in the past from a lack of organised control and supervision over therapeutic substances and medical appliances. The unscrupulous have often reaped a rich harvest at the cost of a long-suffering and ignorant public. Patriotism and love of humanity demand that such exploitation shall cease and I look to the business world to set a high standard of integrity where means for the relief of suffering in particular are concerned.

'I would, however, sound a note of warning to those who consider that legislation and tightening of enforcement are by themselves enough to bring about a healthy tone in public life. What is far more necessary is that the public should develop a sense of responsibility towards their fellow citizens and should co-operate with the authorities in putting down this veritable menace of spurious drugs.

"I like to believe that there has already been an awakening in the minds of the public in this' direction and a realisation of the need for an efficient pharmaceutical profession. I am sure, as pharmaceutical training develops and the trade and profession are manned more and more by people qualified for the purpose, that this evil will automatically be brought under control."

INTERNSHIPS AND RESIDENCIES ABROAD

Applications are invited for Internships and Residencies in U. S. A. and Canada for 1955. The appointments will commence usually from 1st July, 1955. The appointments will ordinarily be paid, but the candidates will have to defray their own passage expenses. The specialities in which Internships and Residencies *may be* available, are as follows:—

1. Pathology and/or Bacteriology, 2. Orthopaedic Surgery, 3. Ear, Nose and Throat, 4. General Surgery, 5. Neurology, 6. Psychiatry, 7. Pediatrics (Children Diseases), 8. Dermatology and/or Venereology, 9. Anesthesiology, 10. Radiology, 11. Internal Medicine, 12. Obstetrics and Gynaecology, 13. Tuberculosis, 14. Ophthalmology, 15. Industrial Medicine.

Applications should reach the State/Territorial Secretaries from the Local Branches of the Indian Medical Association by the first week of September, 1954. Further details obtainable from the Secretaries of the State/Territorial Branches of the Indian Medical Association.

RESEARCH FELLOWSHIPS OF THE INTERNATIONAL CHILDREN'S CENTRE

A number of fellowships for the academic year 1954-1955 will be available for research workers who may wish to work at the laboratories of the International Children's Centre, Paris.

At present the programme of reserch of the Centre is essentially connected with problems of anti-tuberculosis vaccination and antipertussis immunization. The grants amount to 60,000 French francs per month. Travelling expenses from their residence to Paris will have to be borne by the research fellows.

Research workers who wish to apply for a fellowship are requested to send their application together with their curriculum vitae, record of previous work and testimonials of their chiefs of service to Professor Bugnard, International Children's Centre, Château de Longchamp, Paris 16°.

CORRESPONDENCE

The Editor is not responsible for any views expressed by the contributors

COMPLETE ABSENCE OF LEFT LOBE OF THE LIVER

SIR,—I have read with great interest the Case Report of Dr. Reddy of the Complete Absence of the Left Lobe of the Liver in your June issue of the Journal, as this is the first authentic report of such a case in our country. One of the references quoted by Dr. Reddy is the article of E. J. Benz *et al* appearing in *Archives of Pathology*, April 1952. Extracts of the above paper have also been published in Proceedings of the Staff Meetings of the Mayo Clinic, Vol. 28, No. 8, April 22, 1953, in connection with their Symposium on Some Aspects of the Normal and Abnormal Circulation of the Liver.

Dr. Benz and his associates deal with atrophy while Dr. Reddy deals with complete absence of the left lobe of the liver in their respective papers. The two figures published by the former group show that obstruction of the common bile duct with compression of left branch of the portal vein in one case and choledocholithiasis in the second have been operative in the causation of the atrophy. They mention also about the 'capsular wrinkling and prominent biliary and vascular channels" in the atrophied lobe and quote McIndoe and Counseller's suggestion that a dilated left hepatic duct pressing on the long and slender left branch of the portal vein as a probable explanation of some cases of atrophy. Dr. Reddy in his case report has not mentioned anything about the disposition of the vascular structures i.e. Portal V. and Hepatic A. or about the common bile duct though a passing reference is made to "round cell infiltrations around portal areas". It would be perhaps very informative from the paleological aspect to know the condition of the above structures and their anatomical disposition as also that of the splenic vein, as, the streamlining of the vascular supply of the liver is held mainly responsible for the causation of nutritional cirrhosis of the liver and the location of abscesses. I am, etc.,

Bangalore 4. MIRLE PUTTAIYA.

• • • •

SIR,—The absence of the left lobe of the liver was observed only after its severance from the blood vessels and bile tract. As such I was not in a position to indicate the disposition of the vascular structures. I am, etc.

Guntur. D. J. REDDY.

PSYCHIATRY IN GENERAL PRACTICE

SIR,—I remember when as a medical student I first stepped into Waltair mental hospital in the year 1934 my professor Dr. Raghava Rao remarked "gentlemen, you will be surprised to find a small number of lunatics in the asylum. It is not because the incidence of lunacy is so low but because most of the lunatics are outside the asylum. They are still received into your parlour rooms, they join you in your clubs, you look upon them as short tempered or eccentric or impulsive or faddists of this or that or as bores. But most of them ought to be here."

With the rapid urbanisation quick economical and social changes and due to the stress and strain under modern living conditions, cases of pure neurosis like anxiety states, hysteria, neurasthenia and psychosomatic diseases, like hypertension, hyperthyroidism, peptic ulcers, impotence, etc., are rapidly on the increase. The few psychiatrists we have in our vast and yet overcrowded country cannot be expected to cope up with the above volume of work. So the general practitioner attending to ailments occurring in all 'the seven stages of man' has got to play the minor role of psychiatrists.

Firstly one must have the mental picture of a person with sound and normal mental health. A mentally healthy person is at peace with himself and is in comfort, does not succumb to his emotions and impulses; maintains cordial relations with society without effort, plans his future, arrives at his own decisions, becomes wiser with new experiences and uses his failures as stepping stones. With the above knowledge it would not be difficult for one to recognise the neurotic and psychotic personalities when he comes across them. But patients with signs and symptoms of maniac depressive psychosis or schizophrenic or paranoic and paranoid reaction types, are better advised to have admission into institutions as early as possible. Prognosis in all the above

cases has vastly improved of late with recent advances in neurosurgery and improved techniques in convulsion therapy. Diagnosing a mental disease is not very much like diagnosing a case of pulmonary tuberculosis or amoebic dysentery or malarial fever. The above have definite pathologies of their own, of which we have some accurate knowledge whereas most of the socalled mental diseases are but "symptom complexes" but not distinct pathological entities.

Examination of a case with predominantly mental symptoms should be done methodically with special reference to the family history, personal history, past and present; one must watch the patient's behaviour, e.g., general overactivity, stereotyped, automatic obedience, etc.; then one must study the stream of speech, volubility, flight of ideas, relevance, etc., one must note the moods of the patient, whether elated, apathetic or irritable; one must test his memory, note the presence of delusions if any and the sense of orientation. This last feature helps to differentiate neurosis from psychosis, because a neurotic does not lose contact with reality like the psychotic. Presence of delusion indicates psychosis. Depression, irritability, etc., if they cannot be explained by present history, are in favour of psychosis. Insomnia may be present in both but the neurotic finds it difficult to get sleep at first, while the psychotic sleeps ezrly but wakes up soon and finds it difficult to get sleep again. When necessary blood Wassermann test should be done. Having thus arrived at a provisional diagnosis while planning to attend to the chief physical symptoms and giving supportive therapy, adequate nourishment must be given by appropriate routes and good nursing. If the patient is highly excited and irritable sedation should be tried to quieten him.

I prefer to inject paraldehyde up to 7 c.c. intramuscularly or phenobarbitone in appropriate dose may be injected intramuscularly also. Hyoscine hydrobromide or morphine may be given along with it. Paraldehyde 2 to 4 drachms in oil per rectum may be administered. When the patient cooperates sedation by oral route with bromides during day and phenobarbitones at bed time may be continued. Rauwolfia serpentina is a valuable and time honoured drug for these conditions.

When endocrinal disturbances are present suitable substitution therapy should be done.

The confidence of the patient should be gained with frequent chats and kind behaviour and giving him reassurance often about his recovery and a bright future. He may be better shifted to a place more congenial to his temperament and if necessary he may be asked to accept a vocation which he can cope with confidence and ease or to develop a particular hobby to keep him engaged pleasurably. I am, etc.

Tekkali. M. V. RAMA RAO, M.B.B.S.

REVIEWS

DISORDERS OF THE BLOOD—By Sir Lionel E. H. Whitby C.V.O., M.C., M.A., M.D.(CANTAB.), F.R.C.P.(LOND.), D.P.H. and C. J. Britton, M.D.(NEW ZEALAND), D.P.H. J. & A. Churchill, London, 1953. Seventh Edition, pp. 856, Price 63s.

Another edition of this authoritative monograph on blood diseases is most welcome. New chapters include those on haemopoietic metabolism, purpuric and haemorrhagic diseases and therapeutics. The chapter on coagulation of blood includes all recent knowledge on the subject. To the research workers the discourses on cytochemistry and biochemistry of haemopoiesis will be inviting. This is a book for every one seeking advanced knowledge in haematology. However, the reviewer feels that for one working in a tropical country the chapter on infection and infectious diseases is not adequate in essential details.

ATLAS OF EXFOLIATIVE CYTOLOGY—By George N. Papanicolau, M.D., PH.D., Clinical Professor of Anatomy Emeritus, Cornell University Medical College. Published for the Commonwealth Fund by Harvard University Press, Cambridge, Mass. 1954.

This momentous work is a ready reference to all pathologists and those interested in exfoliative cytology. Study of exfoliative cytology is not a new subject, but until exfoliative vaginal cytology was carefully studied by the author of this work and several other investigators its scope was confined to a sporadic examination of an occasional sample of pleural or ascitic fluid with the object of detecting malignant cells in these transudates. During the last thirty years the scope of exfoliative cytology has increased beyond limit, and a book of this kind has been a long-felt want. The literature abounds in scattered observations on the various aspects of the subject dealt with in the book, but as a ready reckoner for the use of a worker in the laboratory this volume is the first of its kind.

The nine chapters in the book can be broadly divided into three sections. The first describes the technique of collecting materials, preparing smears and staining them. Examination of no body fluid is excluded and the individual modifications in technique when dealing with different fluids are carefully considered. This is an extremely valuable section for any laboratory which is organising a cytological unit. The second section deals with general cytological characteristics of malignancy and third with the different regions of the human body to which the study can be extended. These include the female generative system, the urinary and male genital system, the respiratory and digestive systems, pleural, peritoneal and pericardial exudates and breasts. The chapters in this last section are arranged in the form of an atlas which consists of illustrative plates and description, and the value of the atlas is considerably augmented by a short discussion which follows each chapter. These discussions are crisp and learned and provide enjoyable reading. The figures are excellent and in realistic colour. However the reviewer feels that a younger worker would have probably derived more benefit if suitable colour microphotographs were also included in the atlas in addition to the drawings of isolated or cluster of cells depicting the condition.

The book is bound in loose leaf in order to provide for additions to the volume from time to time. This is a great improvement on the standard custom of producing bound volumes which are none too cheap for keeping upto date.

Dr. Papanicolaou is congratulated on this production and the publishers have done justice to it.

It is a volume which every reference library should possess and every pathologist and cytologist should read.

THE ANTISEPTIC. Monthly Journal of Medicine and Surgery. Golden Jubilee number, April 1954.

Founded by Dr. U. Rama Rau in 1904, "The Antiseptic" of Madras, has carved out for itself a place in the

bookshelf of thousands of readers spread all over India and Pakistan. It was very thoughtful and wise on the part of the producers to bring out a Golden Jubilee Number so that the readers may learn, feel and see for themselves, how this monthly journal has come to its present stature from the very modest beginnings, fifty years ago. The proprietor Dr. U. Krishna Rau and the Editor Dr. U. Vasudeva Rau have taken great pains to produce this voluminous number, with a total reading matter of 732 pages full of selections of very good and illuminating articles from the pen of authors drawn from all parts of the vast country—India. This issue will be of great benefit to medical men, specially those who do not have the facilities of consulting a well equipped and up-to-date library.

GESUNDHEIT DURCH KRANKHEIT (Health through Disease)—By H. J. Elechtner: Econ-verlag G.M.B.H.—Dusseldorf, Germany.

There could be no better tribute to the memory of Ehrlich and Behring than a book on immunity. This is such a book, rightly dedicated to Ehrlich-Behring centenary. Written to commemorate the 100th year of their birth, the book displays very well the development of their school of thought through a century, as well as remarkably vivid pictures of these two great men and their colleagues. Presentation is lucid alike to a freshman and a veteran. Yet so much thought is associated with the factual presentations that the book could even be called philosophy of immunity. Outlines of recent developments in immunology are imperceptibly merged with the ground-work laid down by the great immunologists of the 19th century, to make the structure pleasingly well-knit. Selected illustrations, very finely printed in the 16 plates and the 30 figures, which the book contains, adds to the pleasure of reading through the 334 pages of this good book.

THE ECZEMAS—A SYMPOSIUM BY TEN AUTHORS. Edited by L. J. A. Lowenthal, M.D., M.R.C.P., D.T.M. & H. E. & S. Livingstone, Ltd., Edinburgh and London, 1954. Pp. 267, 77 figures—some in colour. Price 35 shillings.

Eczema is a well known term in the theory and practice of the skin diseases. But to the lay public and to many general practitioners it means almost any type of incurable skin disease while to the specialists it often presents a perplexing problem. In this book which is the result of the collaboration of ten well known workers in the lines, an effort is made to solve some of the problems of diagnosis and treatment of eczema. According to the author the term eczema signifies a group of physical signs of inflammatory reaction of a special kind of the skin. The author has made an intelligent classification of eczema and has all the time kept the trends of modern investigation in mind. The author has, however, no more than mentioned the term endogenous eczema, which is the commonest type found in tropical countries. Due importance has not been given to the psychosomatic aspects of the disease though that is the modern trend of thought in its etiology.

The chapters on general principles of treatment and the treatment of various eczemas in detail are very helpful not only to the general practitioners but to specialists as well.

Printing, pictures and get up are excellent.

A TEXT BOOK OF GYNAECOLOGY—By K. M. Masani, M.D.(LOND.), F.R.C.S.(ENG.), F.I.C.S. Published by The Popular Book Depot, Lamington Road, Bombay 7, 1954. Pp. 639 with 261 photographs, microphotographs and illustrations. Price Rs. 17/8/-.

The book is the first of its kind to be written by an Indian author and to be printed and published here. It is a text book catering to the requirements of students preparing for the university degrees.

The printing and the get-up are both good. The illustrations have not all been well reproduced.

OBITUARY

DR. PREMANKUR DE

Dr. Premankur, De, B.SC., M.B., F.R.C.P.(EDIN.), F.N.I., retired Professor of Physiology, Calcutta Medical College and Professor of Pharmacology, Calcutta National Medical Institute, died of coronary thrombosis at his Calcutta residence on July 11 at the age of 62.

He had a brilliant academic career in Calcutta and in Edinburgh, during which he obtained a good number of scholarships including the Ghosh Travelling Fellowship in 1926-27 and Coates Memorial Medal of the Calcutta University for 1946 as the best research worker for the year. He was also elected President for the Physiology Section of the Indian Science Congress held at Bangalore in January 1946.

Connected with various social, educational and cultural organisations, he was loved and respected by all who came in touch with him.

YOUR QUESTION

Correspondents should give their names and addresses (not necessarily for publication) and include all relevant details in the questions which should be typed. Questions of medical interest only will be acceptable for this section. They should be sent in a separate envelop marked. "Your Questions." Questions of general interest will be published in preference. Lack of space precludes answering all the questions received.

Q. What is the latest treatment of myeloid leukaemia?

Ans. Radiography is the best palliative treatment in chronic myeloid leukaemia that has stood the test of time. It can induce repeated remissions, although most cases later tend to become resistant. Treatment must be given under expert direction. Blood transfusion is very useful when the patient is going downhill. Of the drugs arsenic, urethane and folic acid antagonists are now rarely used. More recently urethane has been used by some workers with encouraging results. Nitrogen mustard has also been used; but it has certain disadvantages. Drugs of this type that can be given by mouth have been introduced, but having powerful antihaemopoietic action they must be used under proper haematological control. Radiophosphorus requires special equipment and must be handled by skilled personnel."

Erratum

August 1954 issue, page 483, column 2, para 2, line 4: *in place of* " . . . . 3 followed pulmonary resections . . . " *please read* " . . . . 31 followed pulmonary resections. . . . . "

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SUPPLEMENT

Journal of the Indian Medical Association

VOL. XXIII, NO. 12 CALCUTTA SEPTEMBER, 1954

XX ANDHRA PROVINCIAL MEDICAL CONFERENCE, VISAKHAPATNAM

The XX Andhra Provincial Medical Conference, was held on 19th and 20th June 1954 at Visakhapatnam under the Presidentship of Dr. E. S. Reddy, Nellore. Nearly 500 medical men from all over Andhra attended the Conference. The Governor of Andhra Sri C. M. Trivedi inaugurated the Conference, Sri D. Sanjeeviah, Minister for Planning and Public Health, Government of Andhra inaugurated the Scientific and Medical Exhibitions, and Lt. Col. M. V. Ramanamurti, Director of Medical Services, Government of Andhra inaugurated the Scientific Session and Dr. D. G. Reddy, Principal, Andhra Medical College, presided over it.

While inaugurating the Conference Sri C. M. Trevedi, Governor of Andhra said that the medical men should help in promoting public health and welfare by offering free their services when they had leisure. He also wanted medical men to make their suggestions in regard to the second Five Year Plan. It might be possible to establish a nurses' training college etc. in the Second Five Year Plan period.

Referring to the scarcity of medical aid in rural areas, the Governor said medical men should consider whether it would be possible for them to visit adjacent villages once a week to render aid and make the villagers improve their surroundings. The preventive side was important and doctors could organise lectures and seminars to educate the rural folk on sanitation and hygiene.

Referring to liaison between the Government and Andhra I.M.A. branch, Mr. Trivedi said he was sure it would be welcomed by the Government. In India contacts between the public and medical men were not so close as they were elsewhere. They should consider whether it would be possible to make any headway in this behalf in Andhra State.

Shri D. Sanjeeviah, in declaring open the Pharmaceutical exhibition and the Scientific Exhibition, organised on the occasion indicated that it was not now possible to think of establishing a third medical college in Rayalaseema in view of the poor finances of the State. The Government would certainly welcome the kind of liaison the I.M.A. Andhra branch wanted to establish with the Government. It would be the Government's endeavour to be guided by their suggestions.

Dr. M. V. Krishna Rao, Chairman of the Reception Committee welcomed the delegates and the Governor and in a short speech discussed a few of the urgent needs at the present stage of development of the Andhra State.

The president of the conference, Dr. E. S. Reddy in course of his address said.

"Ours is a declared democratic welfare state. A plan for the economic development is essential. Our leaders have adopted a first five year plan in which prominence is given to river valley projects to overcome deficiency in food and power. They have rightly included some measures for health planning which aim at the creation and maintenance of personnel and community health services on a scale to meet the requirements of the people.

The Health and Development Survey Committee have covered a large field and proposed a long and short term programmes for the re-organisation of the Health Services. Primary Health Centres at the Taluk centres with higher medical services and specialised services at the District Headquarters were recommended. To implement the above, the state and the centre have to commit themselves to heavy expenditure beyond their present capacity to bear. The Planning Commission have therefore suggested re-organisation and readjustment and further expansion of the existing facilities. They laid stress on the expanded preventive work, increase in the number of maternity beds, imparting of health education, family planning and establishment of ante-natal clinics, measures to be adopted during the first five year planning.

MEDICAL RELIEF

The extent of responsibility of the state is determined by the political background of the country. In a socialistic country, the problem is clear. The State is responsible for the production of adequate number of doctors and for their distribution and for their payment.

In order to implement conditions in health planning, more qualified doctors are required. There is at present only one doctor for every fifteen thousand population. Unless we

SHRI C. M. TRIVEDI, GOVERNOR OF ANDHRA, INAUGURATING THE CONFERENCE

treble our number there may not be much hope in the matter of medical relief. Even then the problem may not be solved, unless there is proper distribution of the medical personnel. Though it may not be possible to achieve the ideal as stated in Bhore's Committee report, we have to provide at least one doctor for every 5000 population. This means that we require three thousand and more doctors for our rural population against the eight to nine hundred now available. This shortage in the number of doctors has to be made good by opening additional medical colleges. There are now only two colleges in our State. While thanking the Government for raising the Guntur Medical College to one of full stature, we request for an additional college in this State. The need for the same is acutely felt on account of complete closure of the medical colleges in the Madras State for admission of our boys.

The proposals for a shortened medical course and the shift system have been given up. We thank the Government for

giving up these unhealthy and retrograde measures. There is only one straight road for relieving the present shortage in the medical personnel. That is by opening more medical Colleges. There is great rush for admission. It is a pity to refuse admission for more than 50 per cent of the applicants. The state is responsible for medical education. It is hoped that early measures will be adopted for the remedy of the present state of affairs.

RURAL MEDICAL SERVICE

Our Government have made determined efforts for the last two decades to produce a rural medical service. They have started with a subsidy which is very inadequate and not attractive for medical men to settle down in these remote corners where facilities for education of their children and social amenities are not available. A large number of these subsidised centres have to be closed for want of medical men. The emoluments are poor, there is no guarantee of service and no pension. The doctors to be posted to these rural areas should be full time paid officers with right to pension and other facilities. They may be given further allowance to attract right type of men and to compensate for their hardship in life and extra expenditure for the education of their children.

OUR HOSPITALS AND BED STRENGTH:

The system of medical relief is closely connected with the availability of hospitals and the bed strength. Our hospitals are few and many of them not very well maintained. With the exception of one or two, the other headquarters hospitals have no bed strength of at least 250. None of these hospitals are specialised hospitals. There is only one Civil Surgeon in charge of the both medical and surgical patients. The staff provided is not adequate. The hospitals are overcrowed. It is necessary that specialists should be employed in all District Headquarters hospitals in all branches of medicine and surgery, for consultation and treatment of patients. If the finances of the state are not adequate, recourse may be had for the appointment of honorary Medical Officers and Surgeons who may be paid honorariam to cover their expenditure of transit and other incidental expenditure. It is curious to observe that honorary service though rendered at great sacrifice and inconvenience is little appreciated either by the people or the Government.

There are hardly four thousand beds in all the hospitals of our State. This works out at one bed for every five thousand people. This is very inadequate. There is need for immediate doubling of our bed strength. Even then we will be far below the civilized standard. While it may not be possible to have one bed for every 130 persons as in other civilised countries, we should proceed quickly and provide a bed for every 500 persons. This is a minimum which we should aim at within five to ten years.

MEDICAL EDUCATION

The Medical relief is intimately connected with the medical education that is provided for. One uniform standard of medical education has been recommended by Bhore's Committee. Some states have introduced a hybrid system of medicine. It leads to licensed quackery. It is therefore not advisable to combine two different systems which have no common measure.

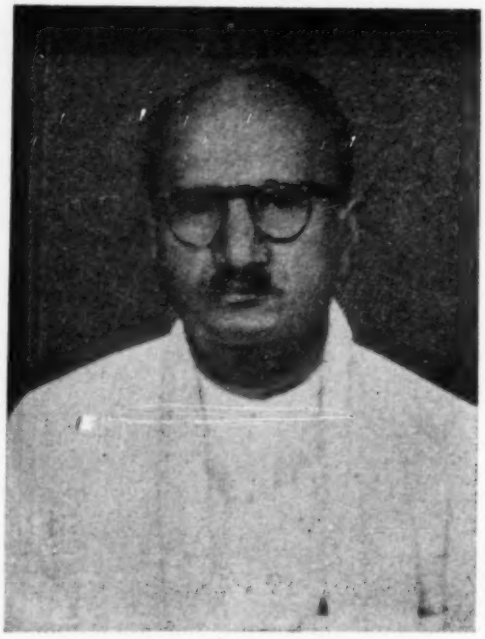
MEDICAL RESEARCH AND POST-GRADUATE TRAINING

Few medical colleges provide facilities for research and post-graduate training. It is necessary that every medical college should have a research section. Mere undergraduate training will not add to the advancement of the medical science. Absence of research may lead to stagnation and may slowly bring about lowering of standards.

There are very few institutions which provide for post-graduate training. Due to lack of facilities, our state and Central Governments have been sending batches of medical personnel abroad for post-graduate medical training. The majority of those sent abroad have only in view the passing of degree and diploma examinations. The chief object of learning post-graduate work is lost sight of. It is high time that our State, Central Government and the University authorities should devise a new policy. Instead of sending medical personnel abroad, young men of merit should be encouraged to undergo post-graduate training and acquire post-graduate qualifications available in this country. Suitable candidates from among these may be selected and sent abroad for holding interships and residencies in well-known hospitals. The experience gained by such trained personnel should not be allowed to run to waste. The Government should utilise their services to the best advantage in our country where there is dearth for such talents.

UP-GRADING OF MEDICAL EDUCATION:

In 1949 the Goversment of India appointed a special Committee to recommend certain centres to be up-graded for specialised studies in certain branches of medicine. As a result of the recommendations, certain departments in some of the medical colleges are being up-graded. The Madras and Stanley Medical Colleges had a fair share in this allocation. In spite of repeated assurances, it is unfortunate that



DR. E. S. REDDY, THE PRESIDENT OF THE CONFERENCE

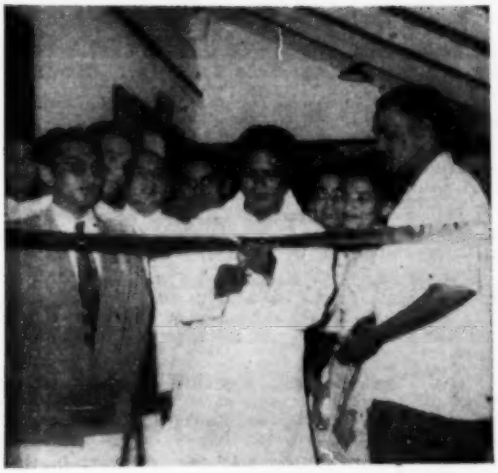
the Vizag Medical College, the only one suitable in our area, has been neglected. I hope this defect will be remedied soon and some departments will be up-graded.

REFRESHER COURSE

Once a candidate passes his examination and takes up an appointment or settles down in practice in the moffusil areas, there are very few chances for him to be in touch with the latest developments in the medical science. With a view to enlarge his knowledge and thereby give benefit to his patients, it is necessary that he is allowed to undergo refresher course for three months once in five years at least at the nearest District Headquarters Hospital which should be well equipped. This is essential in the larger interests of the general public.

OUR NURSES

Much of the success of our hospitals depends on the nursing system that should be provided, and on the ability of our women. Well qualified and highly educated women



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of status should be encouraged to take to the nursing profession. There is at present a kind of apathy and dislike for the profession, though there is none so respectable, no work so ennobling, and so humanitarian. This profession deserves our generous support. The pay is poor and work is so hard that there is no impetus for our respectable girls to take to this profession. We cannot expect selfless devotion of Florence Nightingale or the Roman Catholic nuns in all. The pay and conditions of service must be made attractive.

A degree course in nursing may be instituted to attract educated women to take to this profession. This will be one step in making the profession attractive.

ANTENATAL CENTRES

Organisation of antenatal, natal clinics and establishment of child welfare centres on wider scale are necessary. There is lack of qualified hands, and great reluctance and prejudice are shown by respectable educated girls for this type of work. Better treatment and emoluments may induce many to take to this work in their home areas. Early arrangements have to be made for the opening of a net work of child welfare and maternity relief centres.

PLANNED PARENTHOOD

It may not be out of place to refer to Planned Parenthood. Due to ignorance and superstition there is great opposition to this healthy and well deserving move. A high birth rate which is the result of unplanned parenthood will lead to over-population and a low average life, and hinders economic progress. Every hospital should have a department attached to it to give instructions on the subject to the people. All maternity and child welfare centres should educate our women on the necessity of planned parenthood.

SCHOOL CHILD AND MEDICAL INSPECTION

The children of to-day are citizens of to-morrow. It is highly essential that the child's health should be looked after in all its growth. School children should be periodically examined by competent school medical officers; and any defects, nutritional, physical or mental should be remedied. At present there is no compulsory medical examination of our school children, with the result that the defects and predispositions to disease are allowed to grow. In order to give good facilities favourable for healthy development of our children, a systematic medical inspection should be made compulsory. A small fee, if necessary, may be charged. In this connection I suggest that every school of one thousand and more pupils may be compelled to have a full time or part time medical officer on its establishment. If one school cannot afford it, two or more in the locality may be combined for this purpose. There should be follow up of the child into its adolescence and medical care given for its well being.

PREVENTIVE MEDICINE

May diseases which are contagious and causing high mortality and suffering can be prevented by improvement in environmental hygiene and personal prophylactic methods. Much attention is not yet paid to the primary needs like water, housing and food. Good drinking water is a necessity for life and for the upkeep of health, the supply of which is a primary duty of the state and community. Good housing also is a necessity for the preservation of the health of the community. Unless there is general improvement of sanitation, there can be no improvement of health alround. The state should therefore concentrate on the programmes of water supplies and housing both in the rural and urban areas.

Food is a potent factor in the maintenance of health. For the health and welfare of the community, good and nutritious food must be made available at moderate costs. We are now faced with shortage of protective foods so essential for life and health. Milk so necessary for child's health is in short supply. In a country where there is abundance of cattle, it is a pity that milk should be in short supply, and we are made dependent on foreign imports of milk powders and the like products. It is hoped that when our river valley projects are completed, these deficiences will be overcome.

TUBERCULOSIS AND MALARIA

Two diseases which are due to bad nutrition and sanitation require special mention. These are Tuberculosis and Malaria.

Malaria which is due to bad sanitation can be easily prevented by modern methods of systematic and continued D. D. T. spraying. Once heavy malarial areas like Wynad and Arakh have been made healthy and habitable and more prosperous. Early measures may be adopted for the prevention of this disease which is the cause of a million deaths

LT.-COL. M. V. RAMANAMURTI, INAUGURATED THE SCIENTIFIC SESSION

in our country. For the treatment of malaria, quinine is necessary We produce large quantities of this drug, but not adequate. Steps have to be taken for self sufficiency.

The other disease of great dread and havoc is tuberculosis. Its toll is colossal. It is said that more than one per cent of our population is infected. It may not be possible to isolate all these cases. But every effort should be made for reducing chances of infection by educating the patients and the public in the proper disposal of sputum.

Of late B. C. G. Vaccination has come into prominence. Arrangements may be made for its wide application to protect people from this disease. We are glad to note that the Government are taking efforts to enforce B. C. G. Vaccination.

Sanatoria are necessary for treatment and prevention of the disease. The number now available is inadequate. At least one sanatorium of 200 beds for every district is necessary. The State should encourage private sanatoria by giving 50 per cent building and maintenance grants, besides having their own in select areas. There is only one State Sanatorium of 50 beds in the whole Andhra State. Early arrangements may have to be made to enlarge it.

Tuberculosis is intimately connected with the economic prosperity and nutritional condition of the people. The state must develop the country to increase economic prosperity to give full employment to the community.

As the seeds of this disease are implanted in childhood and signs remain latent till adult life, steps have to be taken for early diagnosis and its prevention. At present, B. C. G. Vaccination is the only available method for its prevention. Early enforcement of this measure is necessary for the interest of the welfare of the community.

COMPULSORY HEALTH INSURANCE

It is necessary that some type of insurance should be introduced for the maintenance of the health of the community. It may not be possible to introduce the scheme on a wide scale throughout in the present state of affairs. In the present shortage of medical personnel and lack of medical relief, the scheme will remain a dead letter. It may be made compulsory in select industrial and urban areas where there is no dearth of medical men. The scheme is said to be working well in Kanpur and Delhi, two important centres. It is time that the scheme should be extended to other areas also. The authorities should be liberal in the matter of compensation to the doctors if the scheme is to work well.

SOCIALISATION

The modern tendency is socialisation of medical services. So far our country is concerned, it may be too early to think of this measure. Where there is shortage of personnel socialisation will not work.

There is only one matter which I would like to stress before I close. It gives me no encouragement to see that many of our brothers have not yet enrolled themselves as members of the Indian Medical Association. I appeal to all to become active members of this association. This association is the most representative national organisation of our medical profession. It is also a member of the World Medical Association. It is only through united front that we can uphold the dignity of our profession.

• • • •

RESOLUTIONS PASSED AT THE CONFERENCE:

I. This Conference urges on the Government of India and Andhra to—

(a) introduce a scheme of State insurance for Industrial employees in the Andhra State (at least in two centres to start with).

(b) introduce a scheme of voluntary health insurance on the basis of a panel system in select urban and suburban areas (to start with) in Andhra State.

II. This Conference urges on the Andhra Government to take up with the Government of India the question of early up-grading of (1) Pathology or any other suitable subject and (2) the history of medicine in the Andhra Medical College.

III. This Conference requests Andhra State Government to take steps to start at an early date special central institutes like Tuberculosis Institute, Public Health Institute, Radiological Institute, Nurses College etc. in the Andhra State to make the state self sufficient in matters of medical research and training.

IV. The President be requested to empanel a Planning sub-Committee to go into the first and second five year plan proposals for Medicine and Public Health in Andhra, to submit a report to the Working Committee of the Andhra Provincial Branch and ultimately to the Government of Andhra.

V. This Conference resolves to request the Government that Honorary Medical Officers be treated on a par with paid personnel in the matter of deputation to foreign countries for obtaining post-graduate training and studies, if necessary they may be asked to give a bond for further Honorary Service for a fixed number of years.

VI. This Conference recommends to the Government to treat the days of journey and attendance of Government and Local Board Medical Officer at I.M.A. meetings either in the District or in the State as on duty instead of treating it as casual leave.

VII. This Conference recommends to the Government for the reservation of 10 per cent of seats in the Medical Colleges for admission to the sons and daughters of the Medical Practitioners and officers in the state.

VIII. This Conference recommends to the Government that the subsidy of the Rural Medical Practitioners of modern medicine may be raised to at least the minimum salary of the Assistant Surgeons for attracting well qualified Medical Men, as the present subsidy is low and unattractive and is an impediment for qualified men to settle down in the rural areas which are devoid of any amenities.

IX. This Conference urges on the Andhra Government to take immediate steps for the constitution of the Andhra Medical Council with its register, and to revise the medical Council Act in consultation with the Andhra Provincial Branch, Indian Medical Association.

XXXI ALL-INDIA MEDICAL CONFERENCE, LUCKNOW

The 31st All-India Medical Conference will be held at Lucknow on the 26th, 27th and 28th December, 1954. The Working Committee of the Indian Medical Association will meet on the 23rd and 24th December, 1954 and the Central Council on the 24th and 25th December, 1954.

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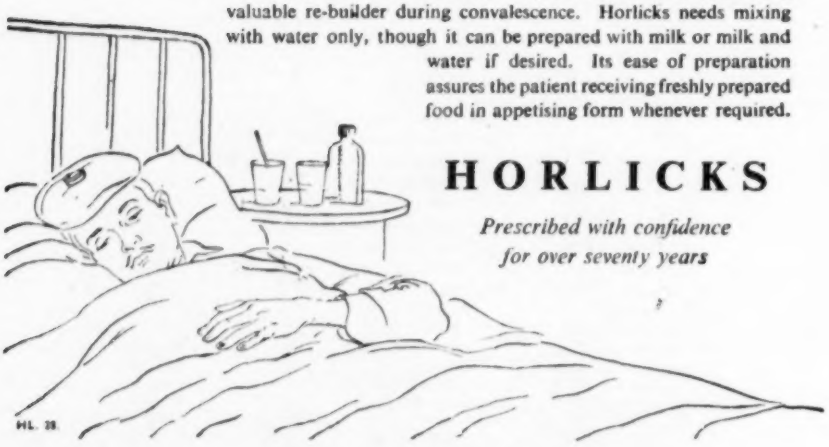

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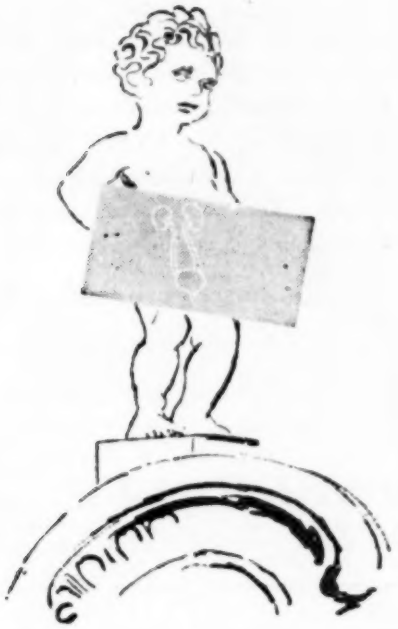

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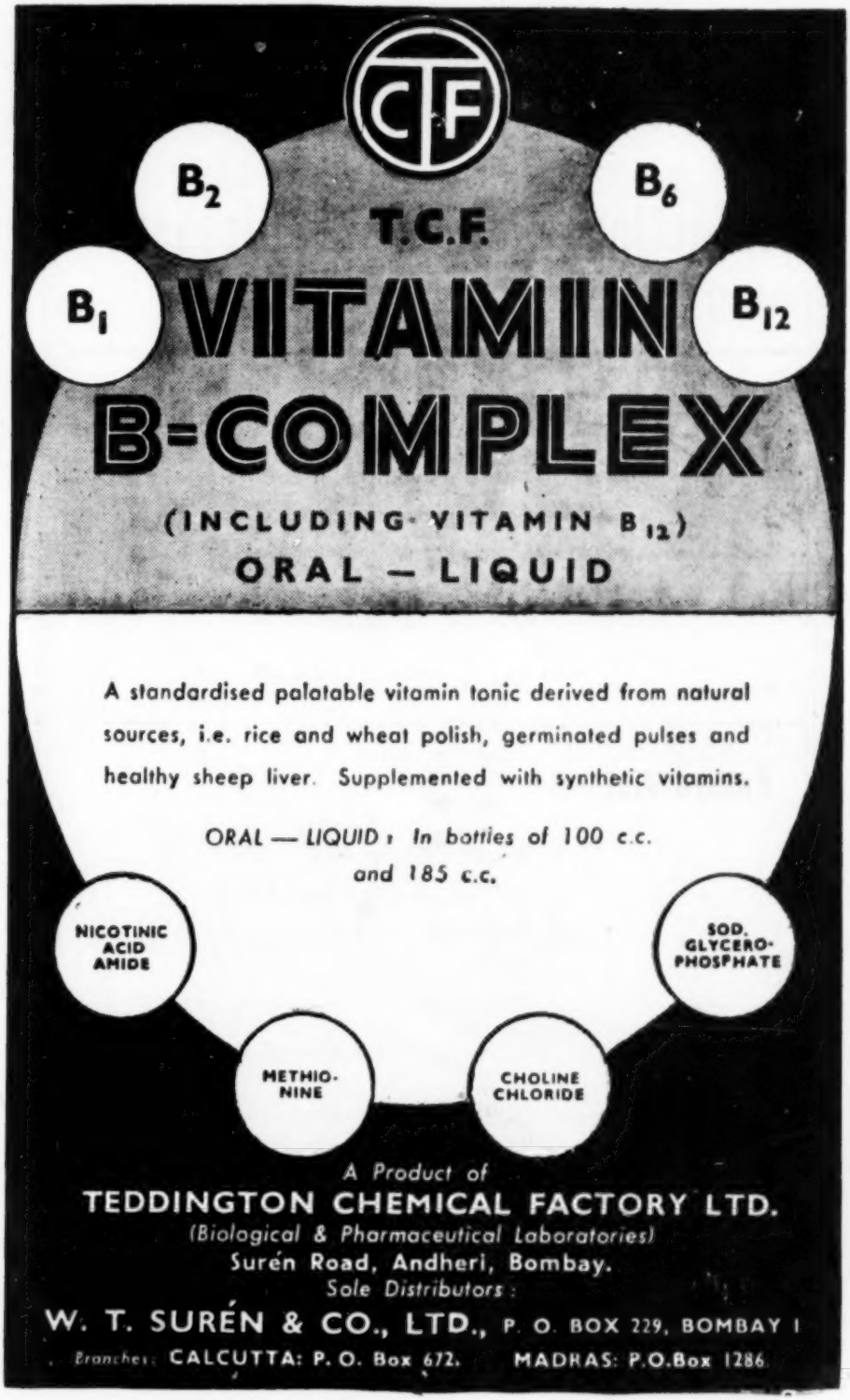
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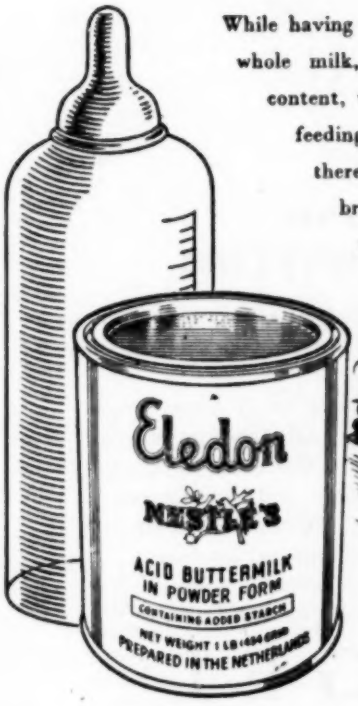

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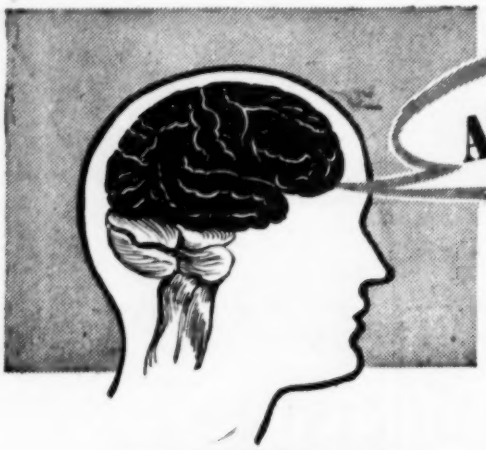

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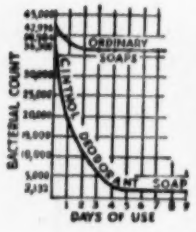

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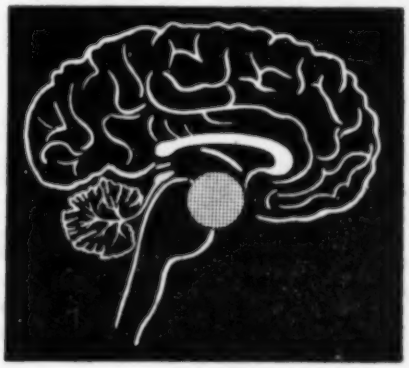

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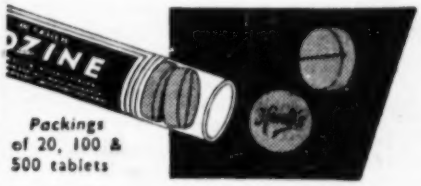

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ANNOUNCEMENT

JOURNAL OF THE INDIAN MEDICAL ASSOCIATION

FORTNIGHTLY

From October 1954

We have much pleasure to announce that two issues of the Journal of the Indian Medical Association would be published every month, one on the 1st and the other on the 16th, with effect from October, 1954.

As General Practitioners form the bulk of the members of the Indian Medical Association, it has been decided to publish for them two articles, specially written by experts, in every ordinary issue of the fortnightly publication, under a new section to be named as "Refresher Course". The section, "Your Questions" is expected to be expanded and made a regular feature, provided the required number of questions are received from the readers of the Journal.

The text of each fortnightly issue would consist of at least 32 pages.

In Special Numbers and whenever occasion arises, the reading matter would be increased as necessary.

The rate of subscription for the Journal would be enhanced from Rs. 18/- to Rs. 24/- per annum from October, 1954. Members of the Association would, however, receive two copies of the Journal every month, without any extra charge.

As the membership of the Indian Medical Association is expected to increase from about 17,000 to 19,000 from October 1954, about 20,000 copies of each issue would be published from October next.

Advertisers of medical products and appliances as well as of other articles which are of use to the members of the medical profession, may avail of the opportunity of advertising their products and articles to the medical profession of India by booking space in the fortnightly issues. For further particulars in this connection, the Hony. Secretary of the Journal of the Indian Medical Association may please be contacted.

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P. K. GUHA
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Fee – £63. 0. 0.

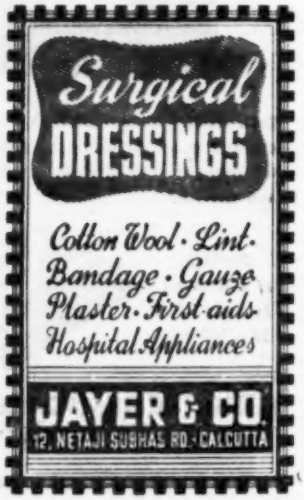
Closing date for applications is Friday, 8th October, 1954.

LECTURES IN ANATOMY, PHYSIOLOGY AND PATHOLOGY, FEBRUARY—MAY 1955

A course of 120 lectures only in the above subjects will be held at the Institute from **21st. February—20th May, 1955.** The Lectures will be held in the Mornings from Monday to Friday each week.

Fee – £36. 15s. 0d.

Full information of and application forms for these courses may be obtained from **Mr. W. F. Davis, Secretary, Institute of Basic Medical Sciences, Royal College of Surgeons, Lincoln's Inn Fields, London, W. C. 2. (HOLBORN 3474)**



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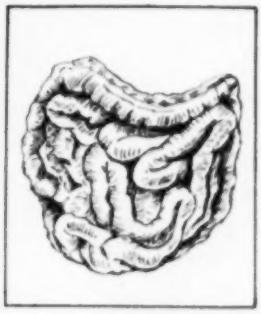

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